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SCIENTIFIC AMERICAN

10 WAYS TO BUILD RESILIENCE

THE SCIENCE OF STRESS

What it does to your brain and body—and how to beat it

INSIDE

How Women Experience Stress Differently

Inequality Is Making Us Sick

Proven Ways to Prevent Burnout

Post-Traumatic Growth

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FROM THE EDITOR

The Pursuit of Resilience

In summer of 2020, in the throes of the global COVID-19 pandemic, researchers at the Centers for Disease Control and Prevention surveyed more than 5,000 adults in the U.S. and found that symptoms of anxiety and depression had increased threefold and fourfold, respectively, compared with 2019. Meanwhile mental health hotlines were reporting surging call rates. And no wonder. The world was grappling with the devastation, fear and uncertainty of a once-in-a-century threat. Acts of racism, violence and political division made the situation profoundly worse.

Stress has immediate cascading effects on the brain, which can be beneficial in some demanding scenarios, such as impending danger. But in the long term, it fuels pathological apprehension and despondency, as Stanford University neurobiologist Robert M. Sapolsky explains in his essential primer that opens this collection (*page 4*). This type of strain runs deep. To wit, a surprising recent finding reveals that even our bones can release a hormone that activates the stress-related fight-or-flight response (*page 18*). And decades of studies show that women and men respond to stress differently (*page 22*), which is important for understanding the ways people cope while under pressure.

Ordinary life stressors are common and can help us to perform better or think faster. But particularly intense or prolonged duress may exact a broader toll: the strain of poverty and inequality can make people sick (*page 48*) and can diminish cognitive performance in children (*page 54*). The coronavirus pandemic has proved to be an unprecedented source of strife. Thankfully, psychologists who specialize in trauma and disaster recovery have a good understanding of the most effective ways to handle extreme circumstances (*page 34*). And researchers are deploying machine learning and other tactics to gather data on the nature of resilience, empathy and coping during and after the pandemic (*page 40*).

Many scientifically vetted methods for self-soothing are reassuringly easy, however. Stanford neuroscientist Andrew Huberman offers simple but powerful tactics that defuse your body's stress response immediately (*page 58*). A few brisk walks during the week can strengthen biochemical hardiness in the body (*page 66*), and even if you're staying home more than usual, mental downtime away from work has a powerful restorative effect on the brain (*page 80*). Backed by clinical evidence, the practice of mindfulness looks to have real chops for rescuing calm and focus (*page 86*).

A substantial proportion of individuals who have survived trauma and turmoil report that their view of life changed for the better in the aftermath (*page 108*). It takes perseverance and determination, to be sure, but an array of tools can help us build our resilience: friendship, goal setting and a positive mindset (*page 94*). These lessons should offer hope in even the most trying times that although stress cannot be vanquished, it can be managed.

Andrea Gawrylewski
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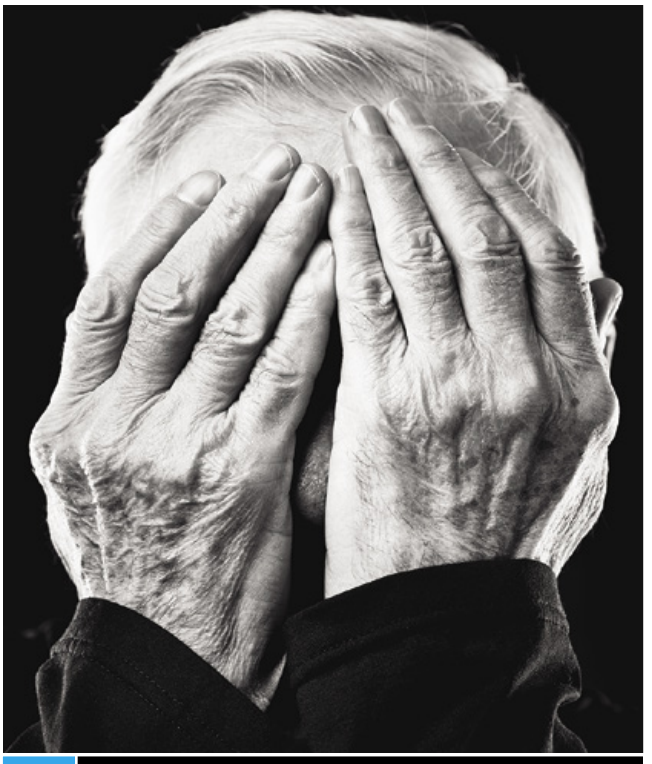

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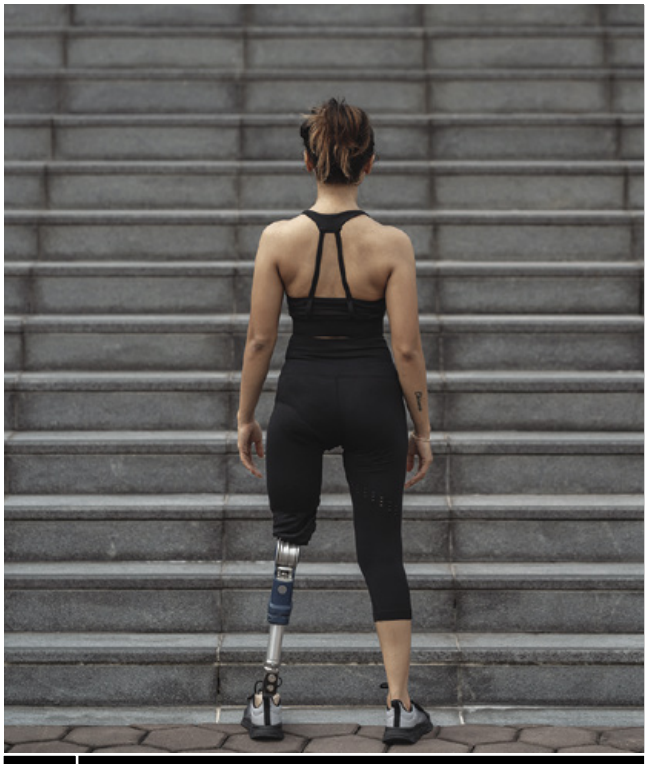

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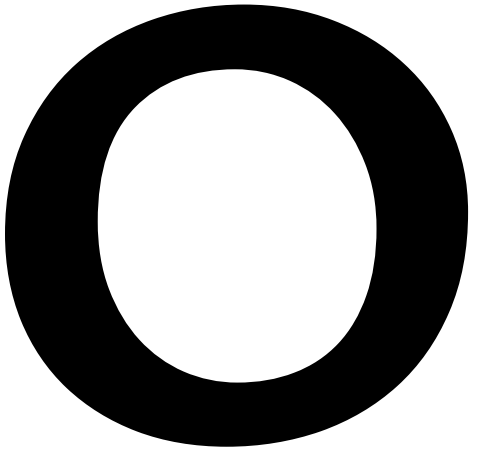
TAMING STRESS

New insights into the neurology of anxiety and depression—and how stress feeds them

By Robert M. Sapolsky



OVER THE CENTURIES TREATMENT OF MENTAL ILLNESS has shifted dramatically. At present, drugs that manipulate neurochemistry dominate therapeutics. In earlier times, the heights of supposed efficacy and compassion were lobotomies and insulin-induced comas. Earlier still, restraints and ice baths sufficed. Go further back, and we enter the realm of exorcisms.

Despite this progress, better treatments are desperately needed, particularly for anxiety and depression. The former, the most common mental illness in the U.S., afflicts 15 to 20 percent of adults in America, and the latter is among the leading causes of medical disability worldwide. Moreover, they were this widespread before 2020; in the COVID-19 era, anxiety and depression have become pandemics of their own.

In this article, I review the brain bases of anxiety and depression (although both words describe everyday transient states that can trouble all of us, throughout I am referring to the medical diagnoses of anxiety disorders and major depression, diseases that incapacitate their sufferers chronically). The study of these ailments readily generates dichotomies: Are anxiety disorders and major depression fun-

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damentally biological or psychological in nature? Do they arise mostly from nature or nurture? But these are false dichotomies, and I will consider here how stress creates links between the neurobiological and the psychological and between genetic and environmental factors. As we will see, although the two classes of diseases differ in their presentations, the role of stress as a risk factor for both reveals their deep similarities.

BIOLOGY OF ANXIETY

ANXIETY COMES in various subtypes, such as generalized anxiety disorder, social anxiety disorder, specific phobias and panic attacks. Despite this heterogeneity, they all involve the serious disruption of normal function by a consistent tendency to see particular circumstances as threats that most other people do not perceive. Given that, it is logical that the brain region whose abnormal function is most implicated in anxiety is the amygdala. This structure is a core part of the limbic system of the brain, a region central to emotions that, while responsive to an array of negative stimuli, is most involved in the perception of and response to fear-evoking stimuli.

Its actions can be highly adaptive. If a lion is stalking you, the activation of the amygdala mediates your appropriate responses to the fearsome circumstance. If your amygdala reacts with the memory of another time that a lion stalked you, its activation helps to consolidate information about what you did to escape. If your amygdala reacts as you approach an African streambed that might harbor a lion, its activation prepares you in case the fear is justified. But if you believe that there will always be a lion waiting for you when you exit an elevator, the activation of the amygdala encapsulates the maladaptive nature of anxiety. This, in turn, can produce a life filled with the corrosive perception of threats to health, safety and well-being that are simply not there.

Unsurprisingly, a consistent finding is that anxiety disorders are associated with chronic hyperactivation of the amygdala and of the brain regions it in turn stimulates—regions involved in the activation of the sympathetic nervous system and its release of epinephrine (also known as adrenaline), along with the secretion of other stress hormones, all preparing the body for fight or flight.

For the amygdala to deal with an ongoing threat, it must receive information about the surrounding world. Such sensory information is first processed in the cortex, which decodes and interprets it, supplying meaning, context and associations before notifying the amygdala. Such integration allows categorization so that, for example, pictures of hands being washed, masked people spaced six feet apart, and a respirator now all trigger the same kind of anxiety in people who endured the stress of 2020.

Crucially, the amygdala also receives sensory information that bypasses the cortex by way of a shortcut. As a result, a potential threat can activate the amygdala before there is conscious awareness of it. This rapid transmission comes with a price: accuracy is sacrificed for speed. This is the world where, with just an instant to react, a cell phone is mistaken for a handgun, and a trigger is pulled. As shown both experimentally and in real life, the likelihood of that mistake varies depending on the race, age and gender of the cell-phone holder, placing the amygdala at the center of an all too familiar relation between bias and tragedy.

The amygdala also receives input from the insula, a region in the brain that processes sensations about the body's internal state (known as interoceptive information)—a stomach rumbling, an achy elbow, a dry mouth before speaking in public. Listening to your heart with a stethoscope unsettles most of us—hearing the beats reminds us of mortality. As shown with neuroimaging, the experience activates the insula, which then activates the amygdala. People with anxiety disorders are especially vulnerable to this phenomenon; greater degrees of insula activation predict greater subjective anxiety. Perhaps this is the neurobiological explanation for those for whom every random twinge of bodily pain suggests a fatal disease.

The amygdala also receives input from additional brain regions. One, the locus coeruleus, uses the neurotransmitter norepinephrine, sometimes called noradrenaline; its activation triggers arousal, alertness and vigilance throughout the brain—particularly in the amygdala. Those with anxiety disorders who experience a typical increase in locus coeruleus activity have exaggerated startle responses.

The amygdala also receives projections from the prefrontal cortex (PFC), a brain region central to executive function, emotional regulation and impulse control. Suppose you were conditioned yesterday to associate a bell with a shock such that by the end of the day, the sound of the bell alone activated your amygdala. But today things have changed: the bell is no longer followed by a shock. At first the ring of the bell activates the amygdala as before. But as the ringing repeats without shocks, the PFC activates, gradually inhibiting the amygdala. Thus, the input from the PFC to the amygdala mediates our ability to discern that we are now safe, extinguishing the amygdala's responsiveness. Not surprisingly, this input is fainter in anxiety disorders; as we will see, a weakened PFC has even more implications.

After this overview, one can appreciate some of the drugs used most often to treat anxiety. Most enhance the potency of the inhibitory neurotransmitter GABA (gamma-aminobutyric acid). It produces a sedating effect, and the drugs used to accomplish this (benzodiazepines such as Valium) are known as minor tranquilizers. Another strategy that has shown some success experimentally, including for the treatment of post-traumatic stress disorder, involves preventing effects of norepinephrine on the locus coeruleus by blocking its receptor with beta-blocker drugs such as propranolol. Some people self-medicate their anxiety disorders by using cannabis, which produces anti-anxiety effects by binding to cannabinoid receptors in the brain, including in the amygdala.

With this brief overview, we now turn to the basic biology of depression, which will prepare us to appreciate the role of stress in the emergence of both disorders.

BIOLOGY OF DEPRESSION BASICS

AS WITH ANXIETY, major depressive disorders come in subtypes, but they all involve a persistent and disabling excess of negative emotions in conjunction with a shortage of positive ones. This imbalance underpins the defining symptom of depression, namely, anhedonia, the inability to feel pleasure. In depression, however, even more fundamental than the inability to feel pleasure is the inability to

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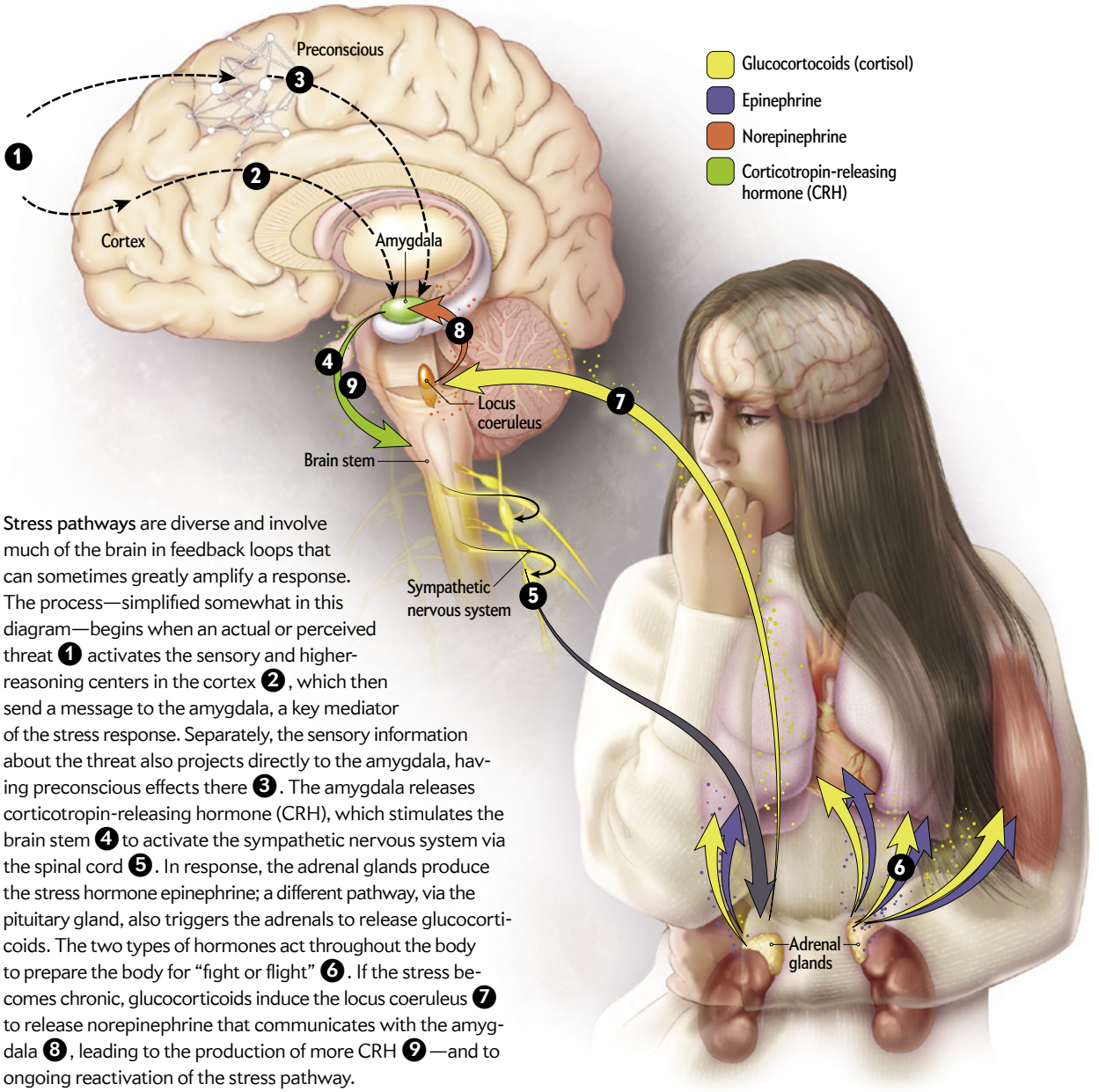
Vicious Cycle of Stress



Stress pathways are diverse and involve much of the brain in feedback loops that can sometimes greatly amplify a response. The process—simplified somewhat in this diagram—begins when an actual or perceived threat ❶ activates the sensory and higher-reasoning centers in the cortex ❷, which then send a message to the amygdala, a key mediator of the stress response. Separately, the sensory information about the threat also projects directly to the amygdala, having preconscious effects there ❸. The amygdala releases corticotropin-releasing hormone (CRH), which stimulates the brain stem ❹ to activate the sympathetic nervous system via the spinal cord ❺. In response, the adrenal glands produce the stress hormone epinephrine; a different pathway, via the pituitary gland, also triggers the adrenals to release glucocorticoids. The two types of hormones act throughout the body to prepare the body for "fight or flight" ❻. If the stress becomes chronic, glucocorticoids induce the locus coeruleus ❼ to release norepinephrine that communicates with the amygdala ❽, leading to the production of more CRH ❾—and to ongoing reactivation of the stress pathway.

anticipate it or to feel the motivation to pursue it. Add to that the symptom of rumination, which in this context means sad thoughts cannot be stopped; the mind churns from one to the next, with interspersed feelings of helplessness and self-hatred. From this pattern comes the classic, poetic characterization of depression as "aggression turned inward" and the tragic suicidality common to the disorder. Concentration, appetite and sleep are typically impaired, and the person becomes mired in "psychomotor retardation," making it exhausting to function in the most everyday ways. High blood levels of glucocorticoids (cortisol in humans), stress hormones secreted by the adrenal glands, are typically found with major depression.

Because anhedonia is at the core of major depression, the neurotransmitter dopamine plays a central part. Although it serves various functions in the brain, the most pertinent is its role in the ventral tegmentum, a region that sends dopamine-releasing projections throughout the limbic system and the frontal cortex. This circuitry was originally termed the dopaminergic reward system, a bit of a misnomer in that the neurotransmitter is even more important for detecting salient cues about the possibility of reward, the anticipation of it, and the goal-

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directed, motivated behaviors needed to attain it. As one might predict, in cases of major depression, this dopaminergic system is less responsive than normal to positive stimuli and cues about reward.

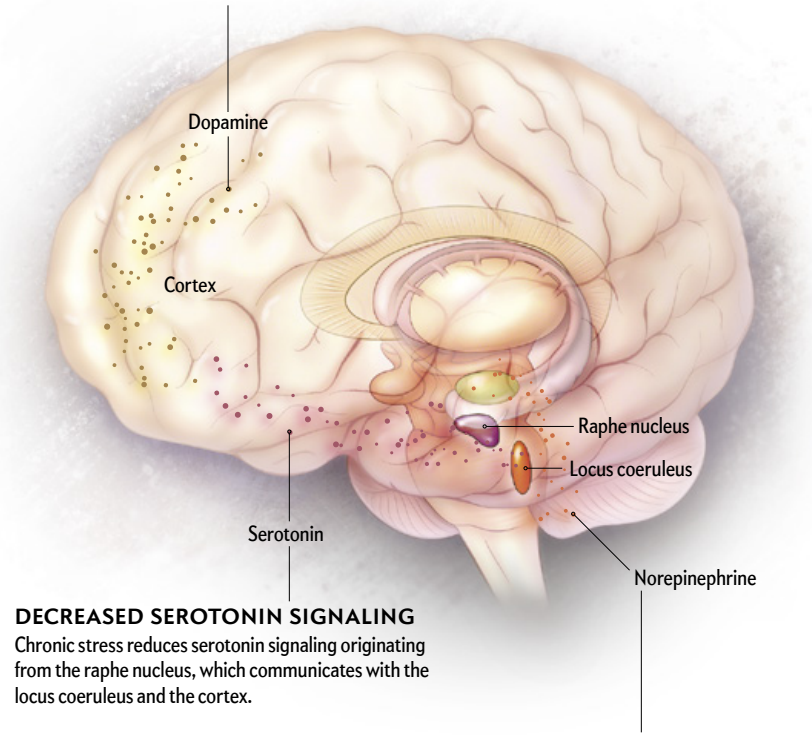
As reviewed, although the amygdala responds to stimuli related to threats, it also responds to other negative stimuli. In major depression, the amygdala is overreactive to various such stimuli, especially those evoking sadness. Although this could be viewed as an amygdaloid function unrelated to fear, one also could reframe this finding in terms of threat. After all, for someone with major depression, few things are as menacing as a stimulus prompting yet more sadness.

Long-term major depression also causes changes in the hippocampus, a brain structure central to learning and memory, namely, atrophy, along with impaired hippocampal-dependent cognition. Pioneering work by the late Ronald S. Duman of Yale University tied these changes to a brain growth factor, brain-derived neurotrophic factor (BDNF), showing in both laboratory animals and humans that depressive states are associated with BDNF shortages in the hippocampus. Moreover, successful treatment of depression with medications reverses the paucity of BDNF, and the efficacy of such drugs might even require this effect on BDNF. Finally, major depression is associated with atrophy and weakened function of the PFC, with, again, depletion of BDNF implicated in the phenomenon (we will revisit the consequences of PFC dysfunction in depression further on).

Depression's Effects

DECREASED DOPAMINE SIGNALING

Chronic stress can increase the risk of depression by blunting dopamine signaling. This neurotransmitter is integral to motivation, anticipation and reward, and it influences multiple brain structures, including the prefrontal cortex.



DECREASED SEROTONIN SIGNALING

Chronic stress reduces serotonin signaling originating from the raphe nucleus, which communicates with the locus coeruleus and the cortex.

DECREASED NOREPINEPHRINE SIGNALING

Because stimulation from the raphe nucleus falls off after chronic stress, the locus coeruleus secretes less norepinephrine, and attentiveness is accordingly diminished.

Along with the underactivity of the dopaminergic reward system, there also appear to be decreases in signaling mediated by norepinephrine and the neurotransmitter serotonin. These changes are the basis for the standard pharmacological strategy for treating depression, that is, using drugs that boost signaling in all three neurotransmitter systems. All block the removal of neurotransmitters from the synapse, allowing them to persist and act longer. The classic examples are the selective serotonin-reuptake inhibitors (SSRIs—drugs such as fluoxetine, sold under the brand name Prozac); dopamine and norepinephrine reuptake also can be enhanced by other drugs such as bupropion. The neurotransmitter glutamate has been implicated in depression more recently: ketamine, a drug that potently blocks a subtype of glutamate receptor, can rapidly lessen severe, intractable depression. Why this works remains mostly unknown; nevertheless, the 2019 approval of ketamine as a treatment for persistent depression by the U.S. Food and Drug Administration represents the first introduction of a new class of antidepressant medications in decades.

BEING OUT OF BALANCE

SO HOW DOES STRESS impact both anxiety and depression?

When a body is in homeostatic balance, measures such as temperature, glucose level, and so on are in the "ideal" range. A stressor is anything in the environment that disrupts homeostasis, and the stress response is the array of physiological adaptations that reestablish balance. Many of these adaptations arise from activation of the sympathetic nervous system and secretion of glucocorticoids.

For most mammals, stressors are acute physical challenges such as evading a predator or pursuing a meal. Epinephrine and glucocorticoids mobilize energy for muscles, increase cardiovascular tone to deliver oxygen and glucose rapidly to those muscles, and inhibit unessential processes such as growth, digestion and reproduction until more auspicious times.

For us primates and other socially sophisticated species, the same stress response can be activated by subtler things than a predator, including thoughts and feelings about other members of our spe-

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cies. This concept brings us to the realm of psychosocial stress. Starting in the 1950s pioneers such as John Mason, Seymour Levine and Jay M. Weiss—then at Walter Reed Army Medical Center, Stanford University and the Rockefeller University, respectively—began identifying key facets of such stress. For the same external stressor, there is a greater subjective sense of stress, a stronger stress response and a higher risk of stress-related disease if there is no outlet for frustration, no sense of control or predictability, no social support and no optimism. Thus, a rat will be less likely to develop an ulcer after a series of mild shocks if it can gnaw on a bar of wood throughout the stressful period as an outlet for frustration. A baboon will secrete fewer glucocorticoids in response to frequent fighting if the aggression results in a rise, rather than a fall, in that baboon's rank in the dominance hierarchy; he will perceive life as improving. A person will become less hypertensive when exposed to painfully loud noise if there is a warning signal five seconds before each blast because she will be receiving predictive information.

But suppose such buffers are not available and the stress is chronic. Repeated challenges may demand repeated bursts of vigilance. At some point this vigilance may become overgeneralized, leading an individual to conclude that she must always be on guard even in the absence of the stress. This person will have entered the realm of anxiety. Alternatively, these insurmountable stressors can produce feelings of helplessness that may become overgeneralized, leading a person to conclude that he is always helpless even when that is not the case. Depression is then upon him.

Thus, we see the links between chronic stress as a psychological phenomenon and the symptomatology of anxiety and depression. This picture fits well with the neurobiological effects of stress.

Sustained stress, by way of excessive glucocorticoid secretion, makes synapses in the amygdala more excitable; furthermore, amygdala neurons grow new connections, even to the point of increasing the amygdala's volume. Moreover, the sensory shortcut to the amygdala that bypasses the cortex is strengthened. Meanwhile glucocorticoids will be having opposite effects in the PFC—reducing synaptic excitability, atrophying neuronal connections, and suppressing the synthesis of BDNF, which would otherwise rebuild those connections. These stress effects produce an amygdala that learns fearful associations more readily and a PFC that is less capable of extinguishing them—our precise neurobiological depiction of anxiety.

As noted, depression is characterized by hyperreactivity of the amygdala (albeit in ways that differ from anxiety) and weakening of the projections to it from the PFC; again, chronic stress and an excess of glucocorticoids bring these changes about. In addition, sustained stress can deplete the locus coeruleus of norepinephrine, with one result being the psychomotor retardation of depression. Most important, chronic stress also impairs the dopaminergic reward system, with evidence for both depletion of dopamine and decreased sensitivity of neurons to it. We now have the neurobiological roots of anhedonia, the loss of anticipation of and the motivation to pursue pleasure.

TRANSITION FROM ANXIETY TO DEPRESSION

THUS, CHRONIC STRESS can produce the neurobiological profiles of both anxiety and depression. But the conviction that threats are everywhere and a feeling of ceaseless sadness are very different emotional states. As we have seen, neurobiologically, anxiety and depression are different malaises. Nevertheless, new insights show their similarities, particularly with respect to the role of stress.

One important commonality is how anxiety can segue into depression. Consider a rat trained to press a lever to avoid mild shocks—a task readily mastered. The anticipatory sense of mastery might well activate the rat's dopaminergic projections to the frontal cortex. And when glucocorticoid secretion is moderate—as would be the case in this scenario—the hormone enhances dopamine release.

Suppose, however, that the lever has been disconnected; pressing it no longer prevents shocks. Initially wildly reactive hypervigilance occurs in the rat as it presses the lever continually or begins other repetitive behaviors, hoping to regain control over the shocks. When these disorganized, frantic behaviors persist long after the shocks have stopped, along with chronic sympathetic activation and elevated epinephrine secretion, we see the essence of anxiety.

But in some rats, as the shocks continue and coping attempts fail, a transition takes place: the coping behaviors stop—the animal has learned to be helpless. The stress response becomes more dominated by high glucocorticoid levels than by epinephrine, and brain chemistry begins to resemble that seen in depression. If anxiety is a crackling brushfire, depression can be a suffocating quilt thrown on top of it.

In other words, anxiety and depression can coexist, with one dominating the other in a context-dependent way. For example, anxiety might come to the fore when one is contemplating a roomful of strangers, whereas depression dominates when that person contemplates global warming. Unsurprisingly, a substantial percentage (perhaps more than 50 percent) of individuals with either disease suffer from both, compounding the therapeutic challenges.

ANXIETY AND DEPRESSION AS COGNITIVE DISORDERS

AS UNDERSCORED by their designation as mood disorders, anxiety and depression are diseases of abnormal emotion. But they are also diseases of abnormal cognition. As pioneered by the renowned psychiatrist Aaron T. Beck (who is celebrating his 100th birthday in 2021), cognitive-behavioral therapy (CBT) focuses on that component of the diseases. CBT aims to uncover the cognitive distortions that lead from a truism of "that happened to me" to the erroneous worldview of "that will always happen to me" and to give the sufferer the cognitive strategies to counter such distortions. CBT is among the most successful psychotherapeutic approaches to the treatment of both diseases, showing the strength of their cognitive components.

The diseases share an additional, related cognitive component. As reviewed, both involve features of a weakened PFC, with decreased metabolism, particularly in the face of enhanced amygdaloid activity, and uncoupling of the ability of the PFC to regulate the amygdala. Depression seems to cause actual cell loss (predominantly of glial cells rather than neurons); anxiety atrophies PFC projections

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to the amygdala (as shown by decreased density of white matter, the insulation around neuronal cables). These various changes are produced by both hyperactivity of the locus coeruleus and glucocorticoid excess.

What are the consequences of a weakened PFC? One classic series of studies (with healthy volunteers) showed the normal functioning of the PFC in this regard. In these experiments, a subject in a brain scanner plays a virtual game of catch on a computer connected to two other "participants" (in actuality, the other two players are part of a computer program). A cyber ball is tossed back and forth among the test subjects; suddenly, for no obvious reason, the other two supposed players snub the human subject and begin tossing the ball just between themselves. In most individuals, this causes a burst of activity in the amygdala, a torrent of negative affect tied to the social insecurities lurking inside us. Then, after a short delay, the PFC typically activates and asserts cognitive control by reappraising the situation ("It's just a game; outside this stupid scanner I have friends and loved ones") and quiets the amygdala.

This is the role of the PFC that is impaired in both disorders. Anxiety and depression can both be thought of as disorders where the PFC is unable to exert cognitive control over adverse emotions. This failure to stop negative thoughts in their tracks leaves the sufferer mired in vicious perseveration on the negative and seems to involve serotonin shortages in both diseases. As evidence, drugs that boost serotonin signaling (such as the SSRIs) ease both anxious and depressive ruminations (as well as the intrusive thoughts and repetitive rituals of obsessive-compulsive disorder).

An insightful definition of depression is that it is the pathological failure of rationalization, and the same applies to anxiety. Whether the wall we put up against the flooding sea is built on facts or on the self-deceptions that often sustain us, its failure in anxiety and depression shows that these are diseases not only of abnormal emotion but also of abnormal regulation of emotion.

CHILDHOOD STRESS AND ITS EPIGENETIC LEGACY

WHEN FACED with chronic stress, only some individuals fall into anxiety or depression. Differing extents of early life stress help explain the differing thresholds for stress-induced mood disorders.

A childhood filled with adversity, trauma or loss can obviously leave scars for a lifetime, including psychiatric ones. Developmental psychologists now formalize such histories with ACE scores (for "adverse childhood experiences"), a tally of a person's childhood experience of physical, emotional or sexual abuse; physical or emotional neglect; and unstable home life because of a family member being incarcerated, addicted, violent or mentally ill. These assessments have revealed a disheartenlingly clear linear relation: the higher a child's ACE score, the greater the likelihood of anxiety or depression in adulthood (along with other heartbreaking outcomes related to educational attainment, antisocial behavior, risky sexual behavior, socioeconomic status and health).

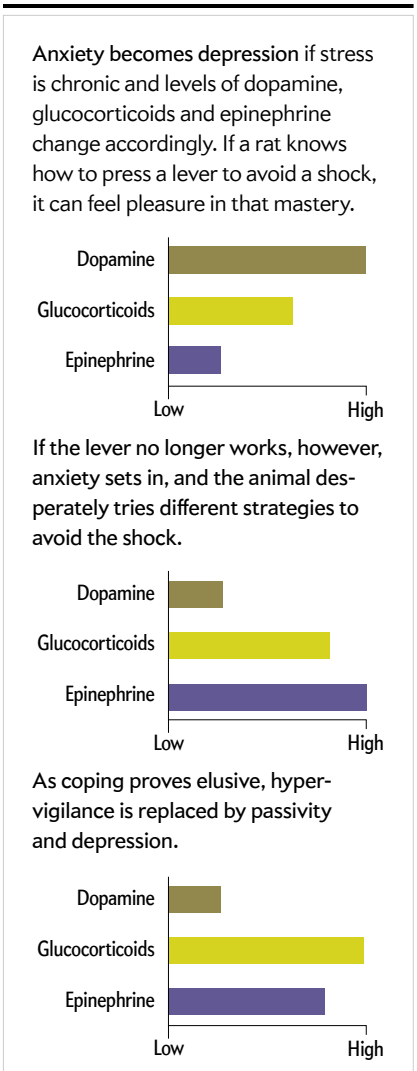
This is no surprise. Childhood is when we first learn answers to two fundamental questions: whether the world is benevolent or malevolent, and whether you can control how your life is turning out. The neurobiological consequences of the answers pertain to at least two domains.

The first concerns how the stressors that make for high ACE scores shape brain development. Sustained childhood stress can impair maturation of the frontal cortex and the hippocampus, prompt the excessive amygdala development that leaves one destined to see threats that are not there, and even decrease the number of dopamine neurons formed. Many of these effects are mediated by excessive glucocorticoid secretion during a stressful childhood.

These effects of stress can also occur during fetal development. Excessive levels of glucocorticoids in the mother's circulation caused by significant maternal stress will elevate glucocorticoid levels in the fetal circulation. When they permeate the fetal brain, these glucocorticoids have damaging effects that are similar to those of glucocorticoid excess in childhood. Environmental effects most certainly do not begin at birth.

Thus, extreme stress beginning in utero and extending into childhood can produce a brain destined to be more vulnerable to anxiety and depression in adulthood. But such childhood adversity alters not only what is, in effect, the hardware of the adult brain but also the software—the very genetic regulation of the adult brain, whose function was established during childhood.

Experience does not change our genes (that is, the DNA sequence that determines the precise protein encoded by each gene). Experience does, however, cause long-lasting or even lifelong changes in the regulation of genes. Such "epigenetic" effects can determine how readily a particular gene in a particular part of the body and in a particular context is activated, thereby determining how much of its cognate protein is made. As first shown by Michael J. Meaney of McGill University and expanded on by other scientists, early-life stress causes epigenetic changes in this article's usual suspects: genes related to serotonin, do-


Anxiety becomes depression if stress is chronic and levels of dopamine, glucocorticoids and epinephrine change accordingly. If a rat knows how to press a lever to avoid a shock, it can feel pleasure in that mastery.
Dopamine
Glucocorticoids
Epinephrine
Low
High
If the lever no longer works, however, anxiety sets in, and the animal desperately tries different strategies to avoid the shock.
Dopamine
Glucocorticoids
Epinephrine
Low
High
As coping proves elusive, hypervigilance is replaced by passivity and depression.
Dopamine
Glucocorticoids
Epinephrine
Low
High

Graphic by Alfred T. Kamajian

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pamine and norepinephrine; to brain sensitivity; to glucocorticoids; and to growth factors such as BDNF. And these are changes that uniformly increase adults' vulnerability to anxiety and depression.

GENETICS AND THE EXPERIENCE OF STRESS

DESPITE THE CRUCIAL IMPACT of early-life stress on adult mental health, many, perhaps even most, people who experience extreme childhood adversity do not develop into adults who suffer from mood disorders. What explains such individual differences?

The answer may lie in genetics. As noted, the DNA sequence that composes a particular gene specifies the precise construction (and thus function) of a particular protein. Crucially, most genes are polymorphic—that is, they come in multiple forms, with small differences in the DNA coding sequences changing the efficacy of the protein produced. This is the rationale for hugely ambitious cutting-edge research into variability across the entire genome in hundreds of thousands of people that aims to identify gene variants that are statistically associated with particular traits. Such studies, known as genome-wide association studies, have produced results of daunting complexity–for example, variants of *hundreds* of genes contribute to a trait as simple as height. Small surprise, then, that genetic surveys have implicated enormous numbers of genes in mood disorders, with none popping out with disproportionate predictive power. Nevertheless, many of the genes implicated are related to now familiar factors: neurotransmitter systems, glucocorticoid signaling and BDNF.

One might conclude, then, that a particular array of gene variants destines someone to inevitably develop a mood disorder. This picture of genetic determinism is wrong, however. Instead there is genetic vulnerability in which the interaction between such genetic profiles and stress, especially in childhood, synergistically increases disease risk.

The classic example was identified in 2003 by Avshalom Caspi of Duke University and his colleagues. They focused on the gene *SLC6A4,* which encodes the serotonin transporter, a protein that removes serotonin from the synapse to terminate its actions. It is a polymorphic gene, and lab studies predicted that one variant would increase the risk of depression. Caspi and his team showed that possessing that variant did indeed have that consequence—but only when coupled with major childhood stress. As further support for this finding, different variants of the gene are regulated differently by glucocorticoids. This variation constitutes a textbook example of a gene-environment interaction, in which the effect of a particular gene variant depends on the environment, and the effect of a particular environment depends on an individual's genetic makeup.

A GENETIC LEGACY OF ANXIETY OR DEPRESSION DOES NOT CONFER A LIFE SENTENCE ON SUFFERERS OF THESE TRAGIC DISEASES.

Despite hundreds of studies concerning this gene-environment interaction, the basic finding about the serotonin transporter is immersed in controversy because it has been less consistently replicated in the most thorough studies with the largest sample sizes. Despite this conflict, it has been a model for an array of subsequent genetic results (personally, I retain faith in the veracity and importance of the original finding). Crucially, variants in a number of our usual-suspect genes predispose us to anxiety or depression, but only when coupled with early-life stress. These are critically important observations.

INTO THE FUTURE

TAKEN TOGETHER, anxiety disorders and depression are diseases of excessive negative affect arising from stress coupled with impaired cognitive control over those negative emotions. An adult's vulnerability to either disorder is increased by early-life stress and its epigenetic consequences. In turn, the impact of early-life adversity is modulated by variability in genes related to vulnerability.

Even with this synthesis, our understanding of the role of stress in anxiety and depression is woefully incomplete. Two issues stand out to me. One concerns the fork in the road separating the two diseases. Not only do anxiety and depression share a framework of genetic vulnerability interacting with early-life stress, but many of the genes and neurotransmitter systems implicated in these diseases (as well as the drugs used to treat them) are the same for both. How can such similar biology give rise to such different outcomes?

There is another domain where more insights are urgently needed. Despite the often bitter exigencies of life, most of us do not succumb to anxiety or depressive disorders, and there are people who are spared despite the most nightmarishly anxiogenic or depressogenic circumstances. It is critical to understand the psychobiology of resilience, which must consist of far more than just the absence of risk factors; this is an area of active research.

Two last take-home messages also come to mind. First, our exploration of the genetics, epigenetics, endocrinology and neurobiology of these diseases underlines the fact that they are *diseases,* as real as, say, diabetes or cancer. This should be recalled by those spared these mood disorders if they are tempted to view a sufferer as self-indulgent or lacking the backbone to just overcome their problems like everyone else does. Finally, it should be self-evident that something is wrong when a society is so unequal as to teach some of its members that life consists of menace and that they are fundamentally helpless; the incidences of anxiety and depression soar among the lower rungs of the socioeconomic ladder. Neuroimaging or genome-wide association studies should not be necessary to make that point palpable. But insofar as they seem to be, findings such as those discussed here should be known far and wide. SA

Robert M. Sapolsky is a professor of biological sciences, neurology and neurological sciences at Stanford University and a research associate at the National Museums of Kenya. In his laboratory work, he focuses on how stress can damage the brain and on gene therapy for the nervous system. He also studies populations of wild baboons in East Africa, trying to determine the relation between the social rank of a baboon and its health.

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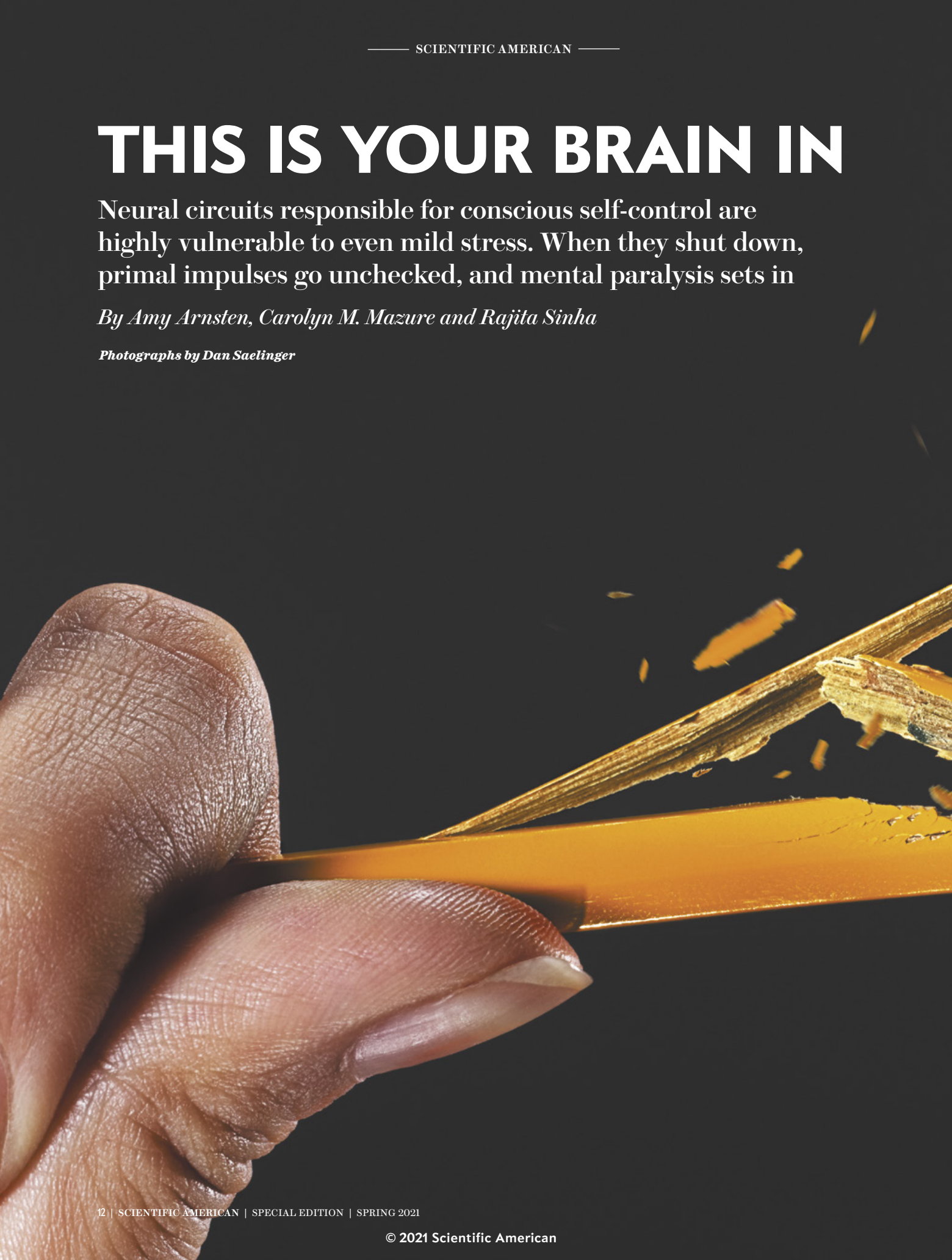
THIS IS YOUR BRAIN IN

Neural circuits responsible for conscious self-control are highly vulnerable to even mild stress. When they shut down, primal impulses go unchecked, and mental paralysis sets in

By Amy Arnsten, Carolyn M. Mazure and Rajita Sinha

Photographs by Dan Saelinger



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MELTDOWN

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THE ENTRANCE EXAM TO MEDICAL SCHOOL CONSISTS of a six-hour fusillade of hundreds of questions that, even with the best preparation, often leaves the test taker discombobulated and anxious. For some would-be physicians, the relentless pressure causes their reasoning abilities to slow or even shut down entirely. The experience—known variously as choking, brain freeze, nerves, jitters, folding, blanking out, the yips or a dozen other descriptive terms—is all too familiar to virtually anyone who has flubbed a speech, bumped up against writer's block or struggled through a lengthy exam.

For decades scientists thought they understood what happens in the brain during testing or a battlefront firefight. In recent years a different line of research has put the physiology of stress in an entirely new perspective. The response to stress is not just a primal reaction affecting parts of the brain that are common to a wide array of species ranging from salamanders to humans. Stress, in fact, can cripple our most advanced mental faculties, the areas of the brain most developed in primates.

Older textbooks explained that the hypothalamus, an evolutionarily ancient structure lodged at the base of the brain, reacts to stress by triggering the secretion of a wave of hormones from the pituitary and adrenal glands, which makes the heart race, elevates blood pressure and diminishes appetite. Now research reveals an unexpected role for the prefrontal cortex, the area immediately behind the forehead that serves as the control center that mediates our highest cognitive abilities—among them concentration, planning, decision-making, insight, judgment and the ability to retrieve memories. The prefrontal cortex is the part of the brain that evolved most recently, and it can be exquisitely sensitive to even temporary everyday anxieties and worries.

When things are going well, the prefrontal cortex acts as a control center that keeps our baser emotions and impulses in check. The new research demonstrates that acute, uncontrollable stress sets off a series of chemical events that weaken the influence of the prefrontal cortex while strengthening the dominance of older parts of the brain. In essence, it transfers high-level control over thought and emotion from the prefrontal cortex to the hypothalamus and other earlier-evolved structures. As the older parts take over, we may find ourselves either consumed by paralyzing anxiety or subject to impulses that we usually manage to keep in check: indulgence in excesses of food, drink, drugs or a spending spree at a local specialty store. Quite simply, we lose it.

The growing understanding that acute stress can severely compromise the function of higher "executive" areas in the human brain has drawn the interest of investigators. They are now not just trying to understand what happens in your head when you freeze but also developing behavioral and pharmaceutical interventions to help you keep your composure.

MIND THE JITTERS

WHY WE LOSE IT has fascinated scientists for decades. After World War II, investigators analyzed why pilots who were highly skilled in peacetime made simple but fatal mistakes in maneuvering their craft during the heat of battle. What actually happens behind the human skull's frontal bone remained a mystery until the relatively recent arrival of neuroimaging techniques. In a brain scanner, the riot of activity in the prefrontal cortex gives a clue to just how vulnerable the brain's master controller is.

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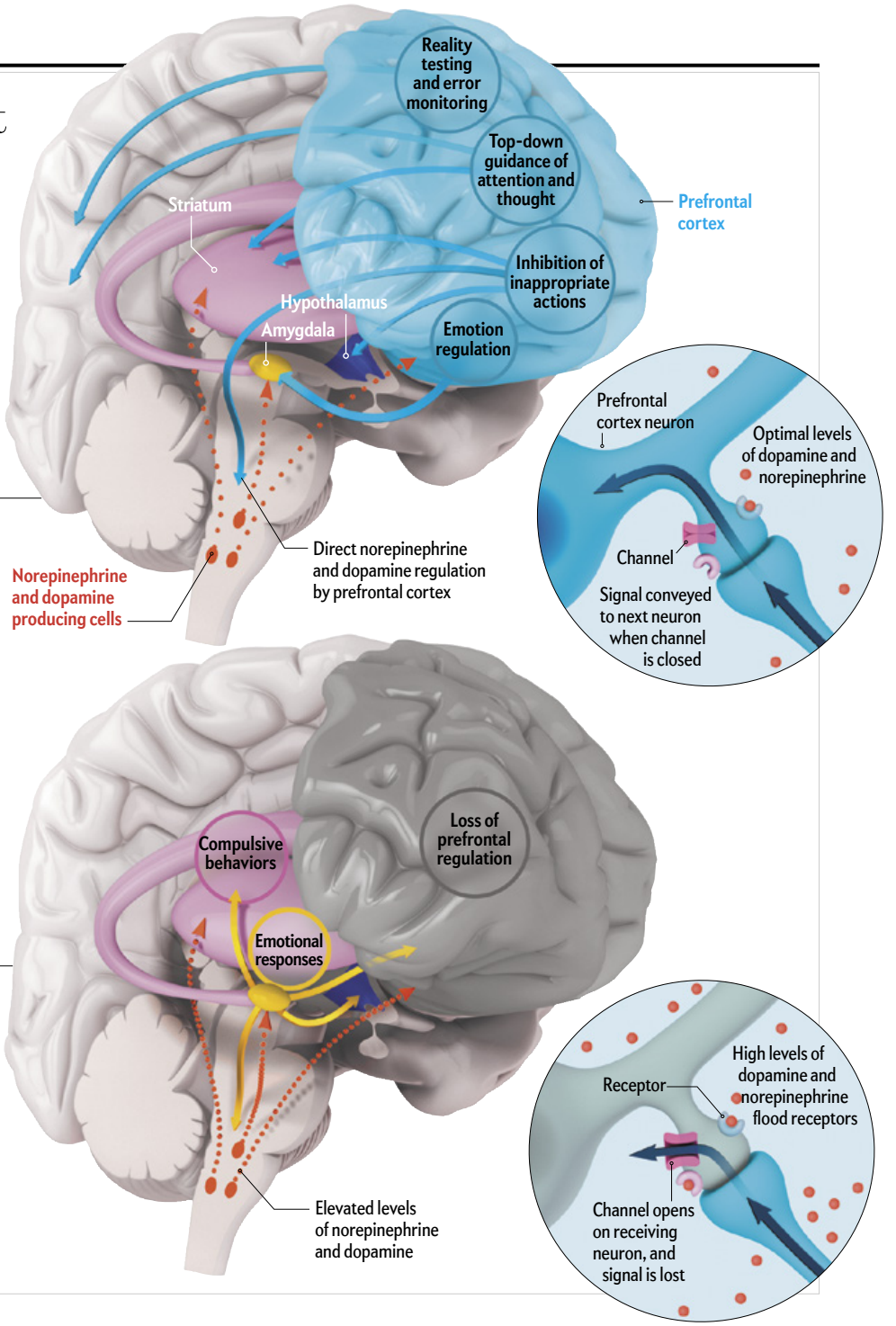
How We Lose It

The area just behind your forehead is the brain's executive control center. The prefrontal cortex, as it is known, is responsible for our ability to inhibit inappropriate impulses. Ordinary, everyday acute stresses are capable, however, of undermining this basic sense of self-control, allowing emotionality and impulsivity to take over.


Reality testing and error monitoring
Top-down guidance of attention and thought
Prefrontal cortex
Striatum
Inhibition of inappropriate actions
Hypothalamus
Amygdala
Emotion regulation
Prefrontal cortex neuron
Optimal levels of dopamine and norepinephrine
Channel
Signal conveyed to next neuron when channel is closed
Direct norepinephrine and dopamine regulation by prefrontal cortex
Norepinephrine and dopamine producing cells
Loss of prefrontal regulation
Compulsive behaviors
Emotional responses
Receptor
High levels of dopamine and norepinephrine flood receptors
Channel opens on receiving neuron, and signal is lost
Elevated levels of norepinephrine and dopamine

Unstressed

Signals from the prefrontal cortex move to areas deep within the brain to regulate our habits (striatum); basic appetites such as hunger, sex and aggression (hypothalamus); and emotional responses such as fear (amygdala). The prefrontal cortex also regulates the stress responses from the brain stem, including the activity of neurons that make norepinephrine and dopamine. Moderate levels of these two neurotransmitters engage receptors that strengthen connections to the prefrontal cortex (*inset*).

Stressed

The amygdala commands the production of excess norepinephrine and dopamine under stressful conditions. That, in turn, shuts down the functioning of the prefrontal cortex but strengthens activity in the striatum and the amygdala. High levels of norepinephrine and dopamine in the prefrontal cortex switch on receptors that open channels that disconnect the links between prefrontal neurons, thus weakening that area's role in controlling emotions and impulses (*inset*).

SOURCE: "STRESS SIGNALLING PATHWAYS THAT IMPAIR PREFRONTAL CORTEX STRUCTURE AND FUNCTION," BY AMY F. T. ARNSTEN, IN *NATURE REVIEWS NEUROSCIENCE*, VOL. 10: JUNE 2009

The prefrontal cortex is so sensitive to stress because of its special status within the hierarchy of brain structures. It is the most highly evolved brain region, bigger proportionally in humans than in other primates, and makes up a full third of the human cortex. It matures more slowly than any other brain area and reaches full maturity only after the teen years have passed. The prefrontal area houses the neural circuitry for abstract thought and allows us to concentrate and stay on task, while storing information in the mental sketch pad of working memory. This temporary memory storage area operates by allowing us to keep "in mind" such information as the sum of digits that need to be carried over to the next column when performing addition. As a mental-control unit, the prefrontal area also inhibits inappropriate thoughts and actions.

The neurological executive center functions through an extensive internal network of connections among the triangular-shaped neurons called pyramidal cells. These neurons also send out connections to more distant reaches of the brain that control our emotions, desires and habits. When unstressed, the circuits in this network hum along contentedly. Working memory reminds us to start that assignment due next week, and other circuitry sends a message to lower brain regions signaling that it is

Illustration by AXS Biomedical Animation Studio

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perhaps best to forgo a second glass of wine. Meanwhile a message to the amygdala, a deep-brain structure that controls fear reactions, provides assurance that the huge hulk approaching on the sidewalk is not about to smash you in the face.

Keeping this network firing as it should can be a fragile process—and when stress hits, even small changes in the neurochemical environment can instantly weaken network connections. In response to stress, our brain floods with arousal chemicals such as norepinephrine and dopamine, which are released by neurons in the brain stem that send projections throughout the brain. Elevated levels of these signaling chemicals in the prefrontal cortex shut off neuron firing, in part by weakening the connection points, or synapses, between neurons temporarily. Network activity diminishes, as does the ability to regulate behavior. These effects only worsen as the adrenal glands near the kidneys, on command from the hypothalamus, spritz the stress hormone cortisol into the bloodstream, sending it to the brain. In this circumstance, self-control depends on a tricky balancing act.

"Keeping one's cool" is an expression that accurately represents the underlying biological processes. The neural machinery of the prefrontal cortex—and its ability to muster working memory to stay focused on the task at hand—may keep the cascade of neurotransmitters generated deep within the brain from triggering a panicked tide of emotion.

Our research clarifying how easily the prefrontal cortex can be shut down started about 30 years ago. Studies in animals by one of us (Arnsten), along with the late Patricia Goldman-Rakic of Yale University, were among the first to illustrate how neurochemical changes during stress can rapidly switch off prefrontal function. The work showed that neurons in the prefrontal cortex disconnect and stop firing after being exposed to a flood of neurotransmitters or stress hormones.

In contrast, areas deep within the brain take a stronger hold over our behavior. Dopamine arrives at a series of deep-brain structures, collectively called the basal ganglia, that regulate cravings and habitual emotional and motor responses. The basal ganglia hold sway not only when we ride a bicycle without falling but also when we indulge in addictive habits, such as those that make us long for that forbidden ice cream.

In 2001 Benno Roozendaal, now at Radboud University in the Netherlands, James McGaugh of the University of California, Irvine, and their colleagues found similar changes in the amygdala, another older brain region. In the presence of norepinephrine and cortisol, the amygdala alerts the rest of the nervous system to prepare for danger and also strengthens memories that are related to fear and other emotions.

"KEEPING ONE'S COOL" IS AN EXPRESSION THAT ACCURATELY CONVEYS THE UNDERLYING BRAIN PHYSIOLOGY.

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This research now extends to humans. These studies have begun to show that some people seem more vulnerable than others because of their genetic makeup or because of a previous history of stress exposure. After dopamine and norepinephrine switch off circuits in the prefrontal area required for higher cognition, enzymes normally chew up the neurotransmitters so that the shutdown does not persist. In this way, we can return to our baseline when stress abates. Certain forms of a gene can weaken these enzymes, making people more vulnerable to stress and, in some cases, mental illness. Similarly, environmental factors can increase vulnerability; for example, lead poisoning can mimic aspects of the stress response and erode cognition.

Still other research focuses on what happens when the assault on the prefrontal cortex lasts for days or weeks. Chronic stress appears to expand the intricate web of connections among neurons in our lower emotional centers, whereas the areas engaged during flexible, sustained reasoning—anything from the philosophy of Immanuel Kant to calculus—start to shrivel. Under these conditions, the branching, signal-receiving dendrites in the primal amygdala enlarge, and those in the prefrontal cortex shrink. John Morrison of the Icahn School of Medicine at Mount Sinai and his colleagues have shown that prefrontal dendrites can regrow if the stress disappears, but this ability to rebound may vanish if

the stress is especially severe. One of us (Sinha) has found evidence of this in humans, where the shrinkage in prefrontal gray matter relates to the history of stress exposure.

This chain of molecular events makes us more vulnerable to subsequent stress and most likely contributes to depression, addiction and anxiety disorders, including post-traumatic stress. Gender appears to be a factor in determining how we react to stress. In women, the hormone estrogen may amplify sensitivity. For example, as one of us (Mazure) and her colleagues have shown, life stress poses a greater risk for depression and is more likely to reduce abstinence from certain addictive behaviors, such as smoking, in women as compared with men. In men, stress may play a more prominent role in exacerbating cravings and eliciting habitual behaviors mediated by the basal ganglia. Reactions that are linked to a specific life stressor are set in a psychosocial context that also can be different for women and men. In ongoing research on frontline health-care workers confronting health risks associated with the COVID-19 pandemic, Mazure and her colleagues are finding that women may have higher rates of stress-related symptoms in response to this experience, and they also have higher rates of concurrent "background stress" such as family or caregiving responsibilities and lower income. This suggests that, for women, biological systems may be chronically on alert, thus presenting an increased challenge in negotiating a significant life stress.

More work on how stress alters the brain's prefrontal self-control locus remains to be done. Some researchers are investigating how other neurochemicals affect the prefrontal cortex. Trevor W. Robbins and Angela Roberts, both at the University of Cambridge, are looking at whether serotonin, which plays a key role in depression, may modulate stress and anxiety through its actions in the prefrontal cortex.

These studies remain challenging because modern ethical standards for experiments using humans state that subjects should not be exposed to situations of extreme psychological stress, and indeed human study participants are told they can stop at any time, giving them control over the experimental situation in a manner that does not mimic real-life stress. Several laboratories have succeeded in simulating the effects of uncontrolled stress by having study participants watch disturbing movies or, as done by the Sinha group, briefly imagine their own stressful experiences to tap into their reactions.

One question that still perplexes researchers is why the brain has built-in mechanisms to weaken its highest cognitive functions. We still do not know for sure, but the triggering of these primal reactions may perhaps have saved human lives when a predatory wild animal was lurking in the bushes. If we suddenly see a tiger burning bright in the forest, it is far more useful to freeze so that the animal cannot see us than to be remembering the words of William Blake's poem.

Absent our slow, deliberate higher-brain networks, primitive brain pathways can stop us on a dime or ready us to flee. These mechanisms may serve a similar function when we face danger in the modern world—say, when a reckless driver cuts us off and we need to slam on the brakes. If we remain in this state, though, prefrontal function weakens, a devastating handicap in circumstances where we need to engage in complex decision-making about a loved one's serious medical condition or organize an important project on a tight deadline.

GET AHOLD OF YOURSELF

A LOGICAL RESPONSE to our growing understanding of the jitters is to devise strategies to keep our neural-control center intact. Scientists hope that understanding the molecular events that cause the brain to degenerate from a "reflective" to a "reflexive" state may lead to better treatments for stress disorders. Some of these insights confirm what we already know. Training for emergencies or for military service is all about teaching the basal ganglia and other brain structures to learn the automatic reactions needed to survive. Animal research suggests that the sense of psychological control that becomes second nature to a soldier or emergency medical technician remains the deciding factor in whether we fall apart during stress. Public speaking exhilarates those who feel confident before an audience. For others, it induces nothing but terror, and their minds "go blank."

The routines of the drill sergeant are mirrored by animal studies that show that juveniles grow up to be more capable in handling stress if they have had multiple, successful experiences confronting mild stress in their youth. Similarly, human studies indicate that success in managing challenging situations can build resilience. In contrast, if children stumble through these experiences, they can become more sensitive to and burdened by stress and depression when they grow up.

Clues to new treatments may be slowly emerging from the lab. The drug prazosin, a generic therapy for blood pressure that blocks some of norepinephrine's detrimental actions, appears to decrease both alcohol cravings and levels of consumption. In 2011 Sherry McKee of Yale and her colleagues found that another generic medication for blood pressure, called guanfacine, can inhibit some stress reactions and strengthen prefrontal cortical networks, helping people to resist smoking during stress exposure. (Arnsten and Yale University received royalties from Shire Pharmaceuticals for an extended-release form of guanfacine used for treatment of attention-deficit hyperactivity disorder for children and adolescents but did not receive royalties for the immediate-release form of the drug used in adults in this study.) Further, many labs have shown that behavioral strategies such as relaxation, deep breathing and meditation can reduce the stress response.

And what about that sense of control? Perhaps by learning about how the brain reacts to stress, you may come away with an enhanced sense of control. So maybe the next time you are taking a test or speaking in public and your mind goes blank, you can say to yourself, "This is just my brain trying to save me from a tiger." Maybe it will bring a comforting smile to your face even if it does not bring the correct answer or word to mind. SA

Amy Arnsten is a professor of neurobiology at the Yale School of Medicine. Her research on molecular changes in the prefrontal cortex during stress and aging has led to treatments such as prazosin and guanfacine for post-traumatic stress disorder, attention-deficit hyperactivity disorder and other conditions.

Carolyn M. Mazure is Spungen Bildner Professor in Women's Health Research and a professor of psychiatry and psychology at the Yale School of Medicine. She created and directs Yale's interdisciplinary research center on the health of women.

Rajita Sinha directs the Yale Stress Center, which focuses on understanding the effects of stress on behavior. She is a professor of psychiatry at the Yale School of Medicine.

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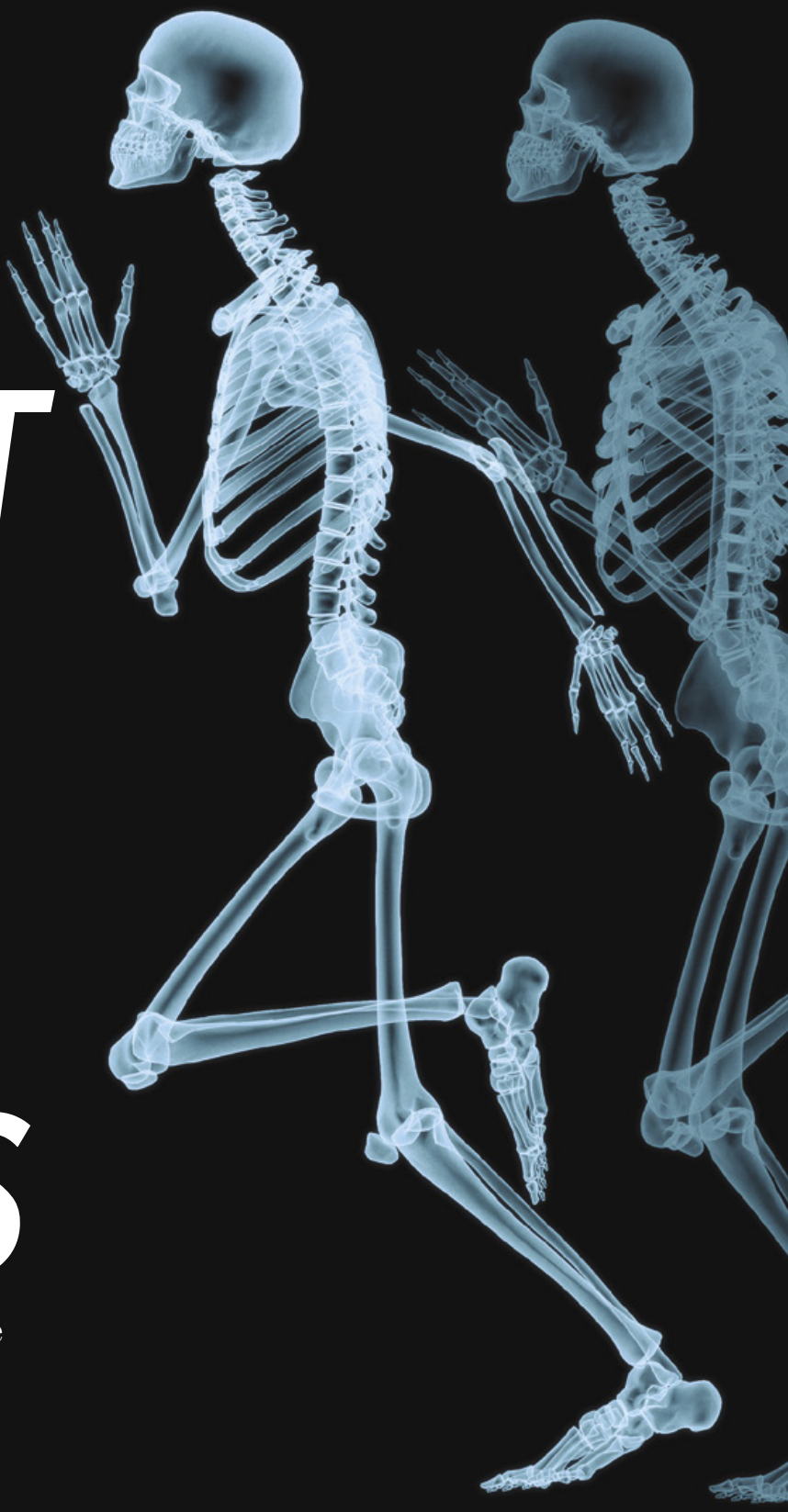
FIGHT OR FLIGHT MAY BE IN OUR BONES



A protein released from bone is involved in triggering the body's reaction to stress

By Diana Kwon

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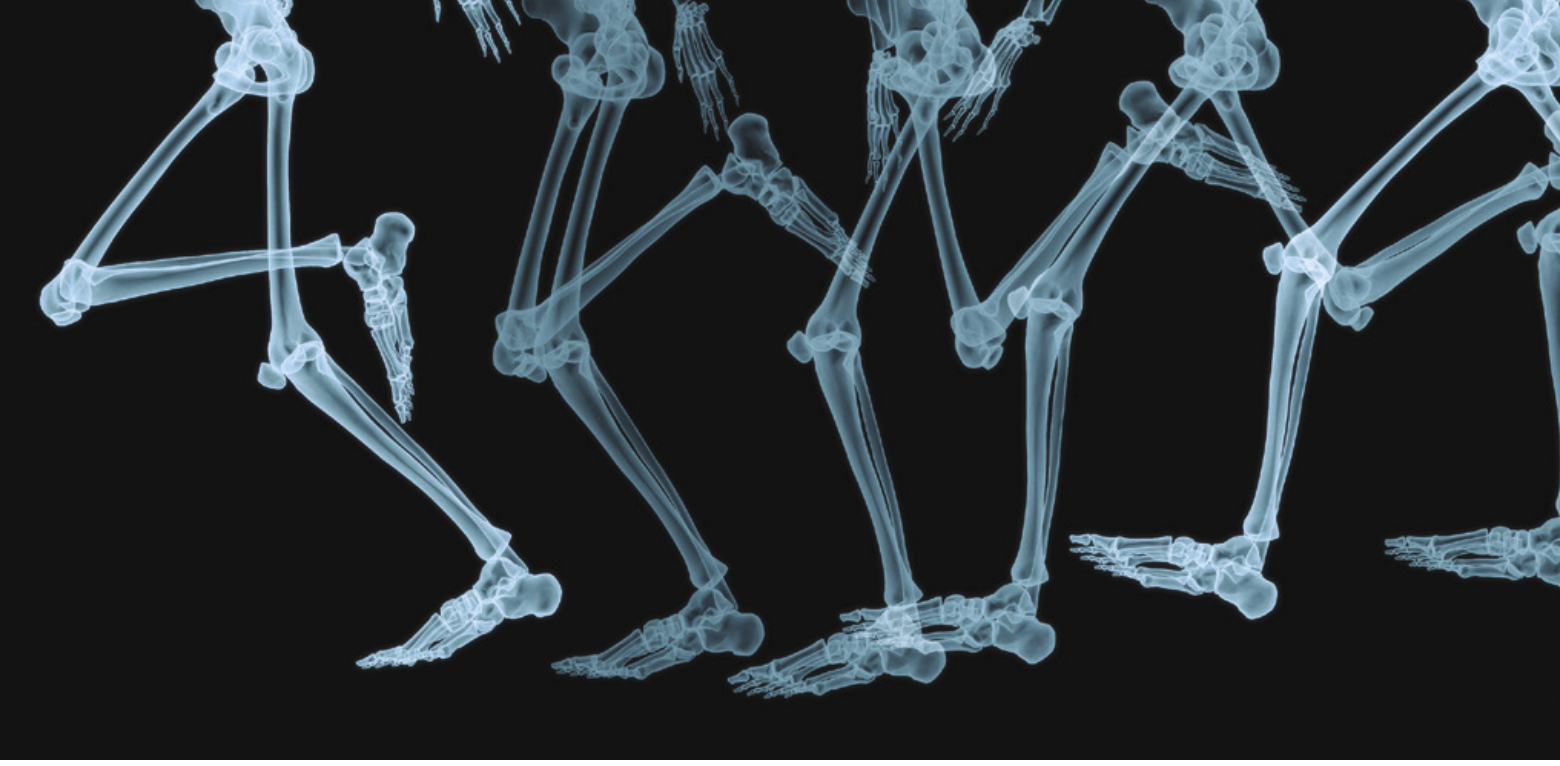

IN THE FACE OF FEAR, WHETHER IT BE CAUSED BY A GRIZZLY BEAR OR AN AUDIENCE waiting to hear you speak, your body initiates a reaction to stress. The breath quickens, the pupils dilate, the heart begins to pound. These automatic responses occur as part of the so-called fight-or-flight response, the body's evolved mechanism to deal with threats around us. Scientists have known for decades that this reaction is triggered by hormones released by the adrenal glands, two cone-shaped organs that sit atop the kidneys. Now a new hormone has entered the picture—osteocalcin, a protein produced and secreted by bone.

Gerard Karsenty, a physician and geneticist at the Columbia University Irving Medical Center, started his work on osteocalcin more than 20 years ago. At first he set out to investigate calcification—a gradual hardening of bone caused by a buildup of minerals. At the time, Karsenty suspected that osteocalcin was a key player in this process because of its abundance in the skeleton. But when his team knocked out the gene coding for osteocalcin in mice, the calcification process remained unperturbed. Instead it found rodents lacking the protein had excess body fat and trouble breeding. These results were perplexing but fit with the fact that osteocalcin is present in blood. That connection led Karsenty to propose that osteocalcin was a hormone released from the skeleton into the blood to help regulate functions in other parts of the body.

The experiment was the first in a long series of studies that identified osteocalcin as a hormone involved in metabolism, fertility and muscle function. Recent investigations have suggested the protein may even play a role in brain development and cognition. As these discoveries accumulated, Karsenty and his colleagues began to wonder why the skeleton, which protects our internal organs and gives us the ability to move, also acts as an endocrine organ with multifaceted roles. This insight led the researchers to the unorthodox hypothesis that perhaps bones evolved, at least in part, to help animals escape from danger. If this idea was correct, then bones might also contribute to the fight-or-flight response.

In a study published in November 2019 in *Cell Metabolism,* Karsenty's team conducted a series of experiments to test this theory. The researchers first exposed both mice and humans to stressful events and measured changes in their blood levels of osteocalcin. In both cases—after the rodents were physically restrained for 45 minutes and after people were asked to give a 10-minute speech—levels of circulating osteocalcin surged. They then knocked out the gene encoding the bone protein in mice and found the animals exhibited a much milder change in physiological fight-or-flight measures, such as increased heart rate, higher levels of blood glucose or a rise in temperature—confirmation that osteocalcin played a critical role in the stress response.

Karsenty's group then dug deeper to probe how, exactly, the hormone influenced the body's immediate reaction to stress. At first, the team suspected that osteocalcin was activating the sympathetic arm of the autonomic, or involuntary, nervous system (ANS), which is responsible for triggering changes associated

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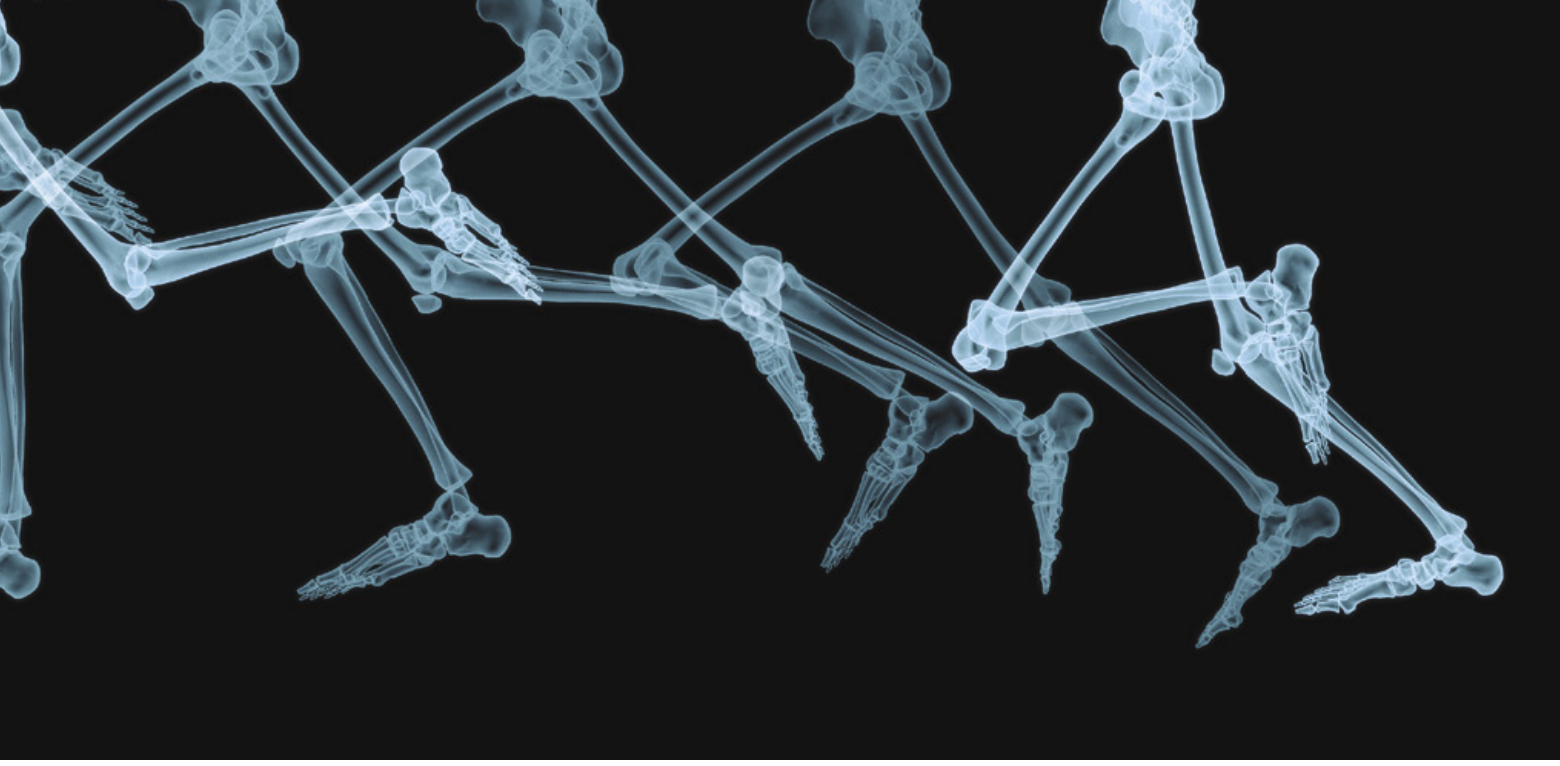

with the fight-or-flight response. But to the researchers' surprise, injecting the protein into the bloodstream appeared to have no effect on the activity of sympathetic nerves. Instead it led to a rapid decrease in activity in nerves of the parasympathetic portion of the ANS, which mediates the "rest and digest" functions that come online when the body is no longer responding to a threat. These findings suggest osteocalcin works by shutting down the ANS, making way for another part of the nervous system to initiate the fight-or-flight reaction.

"The notion that the parasympathetic nervous system is mediating the effects of osteocalcin on stress is a very interesting finding," says James Herman, a neuroscientist at the University of Cincinnati, who was not involved in this work. "I think what that means is that the way we currently understand stress is too simplistic." Herman adds that chemical messengers from other parts of the body may also play a role in the stress response. Experiments from his own laboratory have identified a potential stress-related role for signals secreted from fat.

How osteocalcin communicates with the brain remains unclear, but Karsenty's team has started to address this question. The researchers' paper reports that activating the basolateral amygdala, an area involved in fear processing, led to a twofold increase in osteocalcin levels in the blood. They also identified the neurotransmitter glutamate as a key mediator of the protein's role in the stress response. But Karsenty notes these findings do not provide a clear road map of how the brain-bone cross talk happens. And he does not rule out that other brain regions may be involved.

"Even though we don't understand yet how everything works, I think it's an impressive set of data," says Florent Elefteriou, a professor of orthopedic surgery at the Baylor College of Medicine, who was not part of the study. Whether all these findings translate to humans or end up being clinically relevant remains to be seen, he adds.

Elefteriou, who was formerly a postdoctoral researcher in Karsenty's lab, then at Baylor, notes that the Columbia geneticist has his critics—and that there are members of the bone-research community who have tried and failed to replicate some of his results. (In August 2019, for example, a group of scientists posted a study on the preprint server bioRxiv reporting the absence of endocrine abnormalities in mice engineered to lack osteocalcin, contradicting some of the earlier findings from Karsenty's lab.) "There are people who are in awe in front of these data and think it's exciting, avant-garde, and some people who, because it's so controversial, don't believe a thing," Elefteriou says. "But I think there's still a big chunk of the field who are impressed and enjoy the thought-provoking type of work that's coming out of this lab." SA

"THE NOTION THAT THE PARASYMPATHETIC NERVOUS SYSTEM IS MEDIATING THE EFFECTS OF OSTEOCALCIN ON STRESS IS A VERY INTERESTING FINDING."
—JAMES HERMAN *UNIVERSITY OF CINCINNATI*

Diana Kwon is a freelance journalist who covers health and the life sciences. She is based in Berlin.

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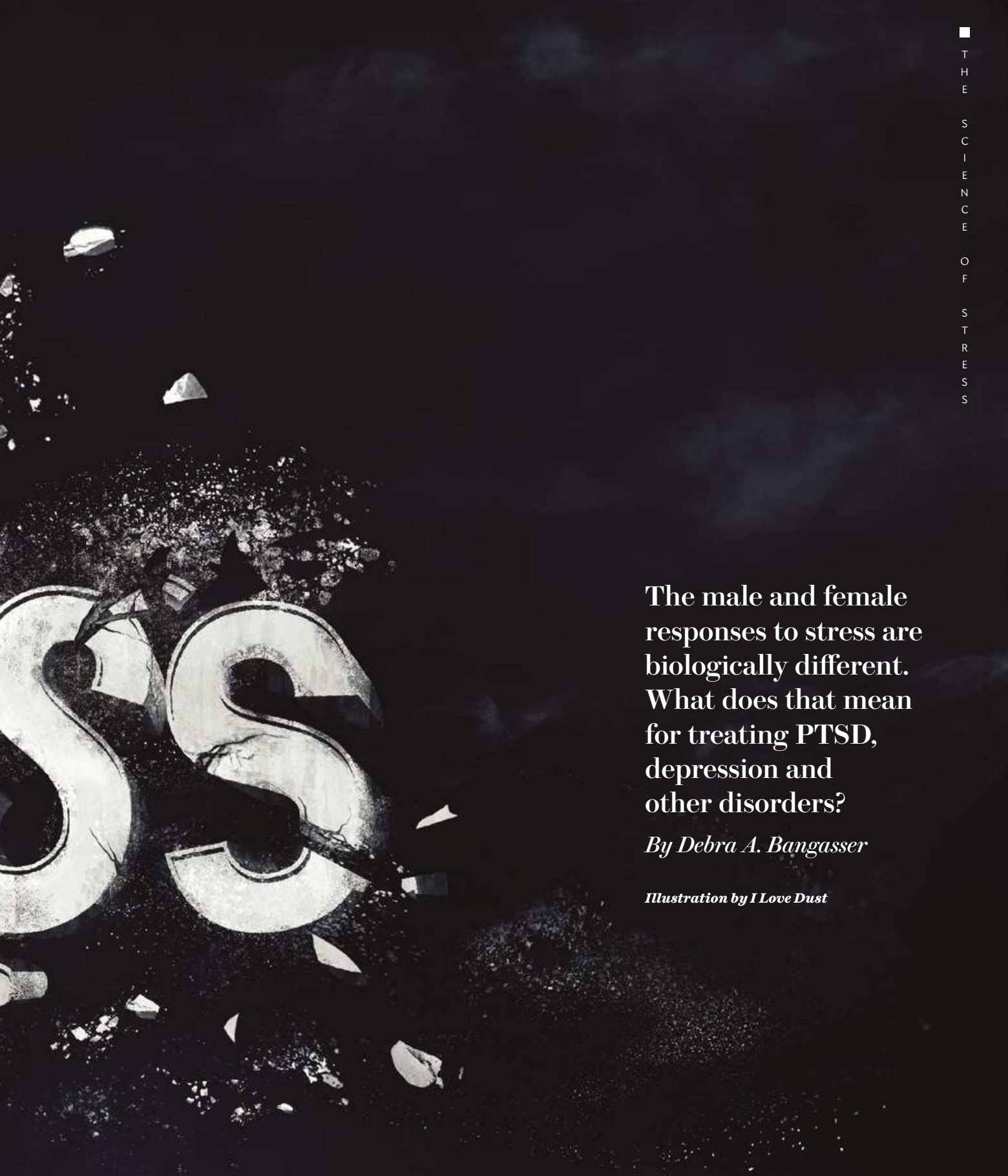

The male and female responses to stress are biologically different. What does that mean for treating PTSD, depression and other disorders?

By Debra A. Bangasser

Illustration by I Love Dust

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THINK ABOUT THE LAST TIME YOU FELT STRESSED. DID YOUR HEART RATE quicken? Did your breathing get shallow and fast? Maybe your muscles tensed, and you became more alert? The brain prompts all these physiological changes to help us survive in the face of a potentially life-threatening situation. But when this response is activated inappropriately or persistently, it can become dangerous. Indeed, research has linked uncontrolled stress to a wide range of health problems, from heart disease and diabetes to depression and post-traumatic stress disorder (PTSD).

Women are roughly twice as likely as men to suffer from stress-related psychiatric disorders, according to epidemiological analyses. The big question has always been: Why? Some experts argue that cultural factors are at least partly responsible. For instance, women may be more willing than men to seek help for mental illness, making their cases more likely to be counted. But evidence from animal research suggests that biology may also play an important role. Scientists are uncovering telling differences in the ways that male and female brains react and adapt to stress.

This insight has been a long time coming. Historically, scientists studied male animals almost exclusively—even when investigating disorders that seem to occur more frequently in women. One reason is that many researchers feared that fluctuating ovarian hormones would complicate their studies, muddy their data and create a need for more subjects or more time at greater expense. Recent investigations have discredited this line of reasoning—the data collected from female animals are no more variable than those from males—but the male bias in animal research has persisted nonetheless.

To address this issue, the National Institutes of Health launched an effort in 2016 in the U.S. requiring that scientists conducting animal studies include sex as a biological variable in their research by studying both male and female animals. As a result, researchers who study chronic stress stand a much better chance of understanding how it impacts the health of both sexes—work that could lead to more effective, sex-specific treatments for psychological disorders. In fact, some of the most promising new therapies under investigation—including oxytocin for anxiety and ketamine for depression—appear to have very different effects in females than in males.

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FEMALE STRESS

THE ANIMAL MODELS scientists use to explore the effects of stress take many forms. Some researchers expose rodents to something stressful—perhaps a brief restraint or a sound they have conditioned the animals to associate with a mild shock—for several days in a row. Others alter levels of stress-related chemicals, such as glucocorticoids or corticotropin-releasing factor (CRF), in the animals' brains via genetic engineering and other techniques. Regardless of the method, many of these manipulations seem to produce faster and stronger reactions in females. We are just beginning to understand why.

It turns out that the most basic cellular processes involved in the stress response differ between the sexes. For example, neuroscientist Georgia E. Hodes, then working in Scott Russo's laboratory at the Icahn School of Medicine at Mount Sinai, conducted a study in which she and her colleagues stressed male and female mice over the course of several weeks. They noticed that it took 21 days to increase anxiety and depressionlike behaviors in male mice but only six days to produce the same reaction in female mice. In search of an explanation, they looked to the nucleus accumbens, a brain region involved in seeking out rewarding and pleasurable activities. Disruption of normal brain signaling in this area is thought to contribute to anhedonia, or an inability to experience pleasure, which is a common symptom in depression and various other stress-related disorders.

Within the nucleus accumbens, Hodes identified sex differences in the regulation of a gene referred to as *Dnmt3a* (DNA methyltransferase 3a). Following a six-day stressor period, it was expressed more in female mice than in males. This gene encodes an enzyme that alters a cell's DNA in such a way that it prevents other genes from being read and used to make proteins. To determine *Dnmt3a*'s role in chronic stress, Hodes removed the gene in the nucleus accumbens of female mice. Without it, the females became more resilient and responded more like male mice. These findings suggest that female mice experience an increase in *Dnmt3a* expression after only a short exposure to stress, which then blocks other proteins that promote stress resilience. Interestingly, researchers are developing drugs that inhibit DNMT enzymes to treat certain cancers. Therefore, similar drugs may be helpful in treating stress-related disorders, particularly in women.

Changes in gene expression are not the only sex differences observed in the brain. When I was a postdoctoral fellow, my mentor, neuroscientist Rita J. Valentino of Children's Hospital of Philadel-

How Scared Is That Rat?

Researchers who study stress in humans can ask their subjects how they feel: Are you stressed, fearful, anxious or depressed? That doesn't work with a rat. Instead my colleagues and I have to try to evaluate a rodent's emotional response to stress indirectly—which means we take careful note of changes in behavior that are thought to reflect fear, anxiety or even aspects of depression. Unfortunately, these behavioral cues were all validated in males and do not necessarily capture signs of stress and fear in females.

In 2015 neuroscientist Rebecca Shansky of Northeastern University and Tina M. Gruene, then a graduate student in Shansky's laboratory, demonstrated that female and male rats have different ways of expressing learned fear. In their experiments, they followed a standard fear-conditioning procedure, teaching rodents to be afraid of a tone by pairing it repeatedly with a mild electric shock to the paw. To gauge how well a rat learns the association, researchers typically measure how much it stops moving (except for breathing) when it hears the tone. The more the rat freezes, the more fearful it is, and the better it has learned—or so the logic goes. But when scientists began testing female rats in the same way, they found that they did not freeze as much as the males did.

Did that mean the females did not learn as well? As it turned out, that does not seem to be the case. With careful observation, Shansky and Gruene noticed that after the conditioning, many female rats darted around their enclosure, perhaps trying to escape. When they considered darting as an indicator of fear, the apparent gap in learning ability disappeared. —*D.A.B.*

GETTY IMAGES

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phia, and I discovered sex differences in receptors that respond to CRF, a hormone that helps to kick-start the body's biochemical response to stress. Although there are CRF receptors in many brain regions, we focused on the locus coeruleus, a structure responsible for changing our levels of arousal from sleepy to fully awake. During a stressful event, CRF floods the locus coeruleus, where it binds to CRF receptors to keep an animal on high alert. Typically these receptors sit on the outside surface of brain cells, waiting for a CRF signal. As CRF levels rise, however, the receptors migrate from the cell membrane to its interior, effectively going off-line. This process is thought to protect brain cells from becoming overactivated.

We discovered that in male rodents, CRF receptors withdrew inside neurons after exposure to a standard stressor. They also withdrew in male rodents that were genetically modified to overexpress CRF. In female rodents, though, the receptors lingered on the cell membrane, where they could remain responsive to high CRF levels. The results suggest that CRF may increase arousal and alertness more in females than in males. In some situations, this difference may actually be adaptive: it can be a good thing to stay fully switched on during a stressful occurrence. But overactivation of this system can also lead to hyperarousal, a disruptive state that, in humans, contributes to insomnia, impaired concentration and feeling inappropriately "on edge."

Patients with PTSD and depression can exhibit high levels of CRF and these symptoms of hyperarousal. So if similar sex differences are found with human CRF receptors, it could help explain why women are more likely to suffer from PTSD and depression. This variation may be hard to demonstrate, however. When human brains are being imaged, technical limitations make it difficult to detect molecular changes such as CRF receptor localization. But we have other reasons to believe that women, like female mice, may have a greater sensitivity to CRF: injecting it into the bloodstream causes a greater rise in stress hormones in women than in men.

THE IMPACT OF HORMONES

WHERE DO THESE DIFFERENCES come from? Emerging research points to the different complement of genes males and females are born with—as well as hormonal surges in the womb and during puberty, both of which can permanently alter the developing brain. Additionally, fluctuating levels of testosterone, estrogens and progesterone can modulate brain function in adults. In my laboratory at Temple University, we assessed the role that these circulating hormones play in regulating rodents' behavioral responses to high levels of CRF by looking at compulsive grooming.

When a rat compulsively licks its own fur, sometimes to the point of causing baldness, it is thought to reflect a state of high anxiety. The compulsive grooming may be a form of self-soothing. We found that when we injected CRF into rats to induce stress, females engaged in more compulsive grooming than males did. Moreover, the amount of grooming changed over the course of a female's estrous cycle, which is similar to the human menstrual cycle but lasts only four to five days. At the phase of the cycle when ovarian hormones—including estrogens and progesterone—peaked, CRF triggered even more compulsive grooming, suggesting that the hormones somehow amplify CRF's effects.

Behavioral responses such as grooming draw on many brain regions. So in trying to account for the grooming differences between the male and female rats, Kimberly Wiersielis, then a graduate student in my lab, speculated that CRF might activate different circuits in their brains. To test this idea, she examined brain slices for cFos, a protein expressed only when brain cells are switched on. Then we statistically compared cell-activation patterns. Our analysis revealed that CRF activated diverse brain regions in both

A Heavier Toll for Women

Women are more likely than men to be diagnosed with a psychiatric disorder related to stress, with the exception of substance abuse. This discrepancy may be partly because of social factors, such as males' reluctance to seek help. But it probably also reflects biological differences in how male and female brains respond to stress.

Lifetime Prevalence (percent)

DISORDER	FEMALE	MALE
Major depression	20.2	13.2
Migraine	18.2	6.5
Irritable bowel syndrome	14.5	7.7
Insomnia	12.9	6.2
PTSD	9.7	3.6
Alcohol abuse	7.5	19.6
Generalized anxiety	7.1	4.2
Panic	6.2	3.1
Drug abuse	4.8	11.6

SOURCE: "SEX DIFFERENCES IN STRESS-RELATED PSYCHIATRIC DISORDERS: NEUROBIOLOGICAL PERSPECTIVES," BY DEBRA A. BANGASSER AND RITA J. VALENTINO, IN *FRONTIERS IN NEUROENDOCRINOLOGY*, VOL. 35, NO. 3, AUGUST 2014

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sexes, but the patterns were different—and especially so between males and females at the point during estrus when females have the highest levels of estrogens and progesterone.

A SEX-BASED RX

THESE SEX DIFFERENCES are not minor. As we search for better remedies for stress-related psychiatric conditions, it is vital that we take them into consideration. To date, potential therapies are most often screened in male rodents. But the same compounds can have very different effects in females. For example, neuroscientists Brian Trainor and Michael Q. Steinman, then both at the University of California, Davis, tested one putative therapy, oxytocin, in both male and female mice. Because this hormone promotes social bonding in mammals, scientists have speculated that administering it to people in the form of a nose spray might reduce social anxiety and avoidance, as well as improve deficits in processing social cues, a problem that is seen in some people who have stress-related psychiatric disorders. Their group found that intranasal oxytocin did indeed reduce anxiety in male mice, but it made female mice even more anxious under certain conditions. We need to make sure that oxytocin sprays will not cause similar adverse side effects in women.

Ketamine provides another example. This medication, normally used as an anesthetic, blocks the *N*-methyl-D-aspartate receptor, a protein that can regulate many processes, including aspects of the stress response. It has generated a lot of excitement as a potential therapy for depression because, unlike traditional antidepressants that can take weeks to provide any benefit, low doses of ketamine reduce symptoms fast, sometimes after a single infusion. Unfortunately, high doses of ketamine can induce delirium, hallucinations and an "out of body" experience (which is why it is also a popular recreational drug).

Researchers have been investigating ketamine in male animals to develop more targeted therapies for depression. In 2013, though, neuroscientists Mohamed Kabbaj of the Florida State University College of Medicine and Nicole Carrier, then a graduate student in his lab, also tested ketamine in female rats. They found that it took less ketamine to relieve depressionlike symptoms in the females and that it was not just a matter of differences in body mass. Instead a different biological mechanism seemed to be at work. If these same differences exist in humans, researchers working on new drugs with ketaminelike properties may need to develop separate therapies for men and women. Researchers continue to evaluate ketamine for its long-term safety and effectiveness, and these studies may well reveal that, like female rats, women should receive a lower dose. (In 2019 the Food and Drug Administration approved a ketaminelike drug, called esketamine, for use against treatment-resistant depression.)

We do not know why males and females would have evolved different biological responses to stress. One possibility is that a female animal protecting vulnerable young might be well served by being able to maintain a heightened state of alertness and awareness of her surroundings—as would her babies. That advantage might outweigh the downstream risks associated with increased stress sensitivity, such as greater vulnerability to depression and anxiety disorders. Studies are needed, however, to investigate this idea.

OUR PAST RELIANCE ON MALE ANIMALS IN DRUG-DEVELOPMENT STUDIES MAY EXPLAIN, AT LEAST IN PART, WHY WOMEN REPORT MORE ADVERSE DRUG REACTIONS THAN MEN DO.

As we commit to including female animals in research, we stand to learn more not only about disorders that are more common in women but also about conditions that are more often diagnosed in men, such as autism and attention-deficit hyperactivity disorder. In this case, looking at brain differences in females might reveal factors that confer greater resilience. Better-targeted treatments for both sexes could follow.

It is becoming increasingly clear that the traditional approach of studying only male animals is flawed. In fact, our past reliance on male animals in drug-development studies may explain, at least in part, why women report more adverse drug reactions than men do. The practice may also have kept drugs that would be highly effective in females from ever making it to market. The good news is that thanks to new efforts that promote the study of both male and female animals, change is underway. SA

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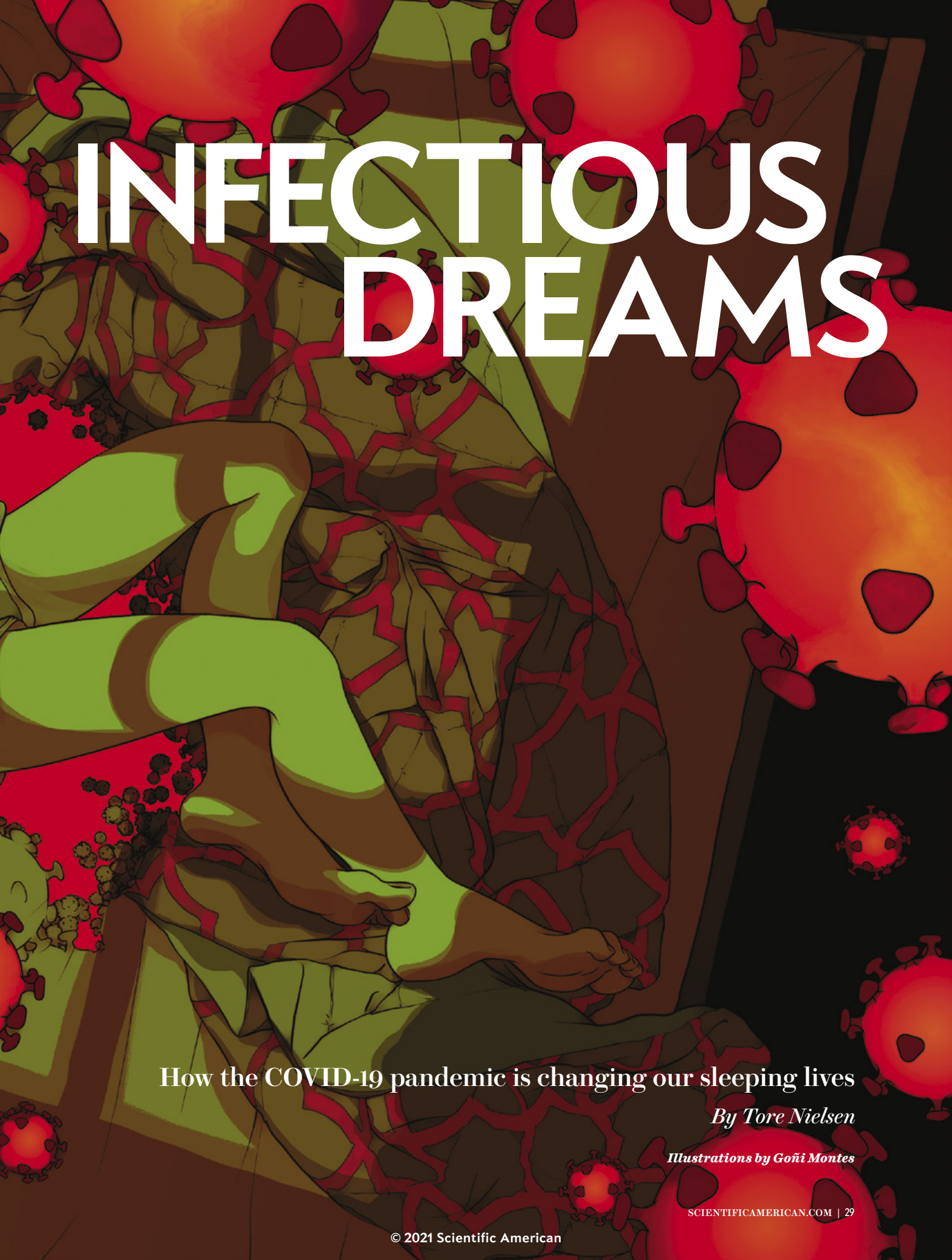

INFECTIOUS DREAMS

How the COVID-19 pandemic is changing our sleeping lives

By Tore Nielsen

Illustrations by Goñi Montes

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FOR MANY OF US, LIVING IN A COVID-19 WORLD FEELS AS IF WE HAVE BEEN thrown into an alternative reality. We live day and night inside the same walls. We fear touching groceries that arrive at our doorstep. If we venture into town, we wear masks, and we get anxious if we pass someone who is not wearing one. We have trouble discerning faces. It's like living in a dream.

COVID-19 has altered our dream worlds, too: how much we dream, how many of our dreams we remember and the nature of our dreams themselves. In early 2020, when stay-at-home directives were put in place widely, society quite unexpectedly experienced what I am calling a dream surge: a global increase in the reporting of vivid, bizarre dreams, many of which are concerned with coronavirus and social distancing. Terms such as coronavirus dreams, lockdown dreams and COVID nightmares emerged on social media. By early April of last year, social and mainstream media outlets had begun broadcasting the message: the world is dreaming about COVID-19.

Although widespread changes in dreaming had been reported in the U.S. following extraordinary events such as the 9/11 attacks in 2001 and the 1989 San Francisco earthquake, a surge of this magnitude had never been documented. This upwelling of dreams is the first to occur globally and the first to happen in the era of social media, which makes dreams readily accessible for immediate study. As a dream "event," the pandemic is unprecedented.

But what kind of phenomenon is this, exactly? Why was it happening with such vigor? To find out, Deirdre Barrett, an assistant professor at Harvard Medical School and editor in chief of the journal *Dreaming,* initiated a COVID-19 dreams survey online in the week of March 22, 2020. Erin and Grace Gravley, San Francisco Bay Area artists, launched IDreamofCovid.com, a site archiving and illustrating pandemic dreams. The Twitter account @CovidDreams began operation. Kelly Bulkeley, a psychologist of religion and director of the Sleep and Dream Database, followed with a YouGov survey of 2,477 American adults. And my former doctoral student Elizaveta Solomonova, now a postdoctoral fellow at McGill University, along with Rébecca Robillard of the Royal's Institute of Mental Health Research in Ottawa and others, launched a survey to which 968 people aged 12 and older responded, almost all in North America. Results of these inquiries, published in *BMJ Open* in December 2020, document the precipitous surge, the striking variety of dreams and many related mental health effects.

Bulkeley's three-day poll revealed that in March 2020, 29 percent of Americans recalled more dreams than usual. Solomonova and Robillard found that 37 percent of people had pandemic dreams, many marked by themes of insufficiently completing tasks (such as losing control of a vehicle) and being threatened by others. Many online posts reflect these findings. One person, whose Twitter handle is @monicaluhar, reported, "*Had a dream about returning as a sub teacher in the fall, unprepared. Students were having a difficult time practicing social distancing, and teachers couldn't stagger classes or have one-on-one meetings.*" And @therealbeecarey said, "*My phone had a virus and was posting so many random pictures from my camera roll to instagram and my anxiety was at an all time high.*"

More recent studies found qualitative changes in dream emotions and concerns about health. Dream reports from Brazilian adults in social isolation had high proportions of words related to anger, sadness, contamination and cleanliness. Text mining

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of accounts of 810 Finnish dreams showed that most word clusters were laden with anxiousness; 55 percent were about the pandemic directly (lack of regard for social distancing, elderly people in trouble), and these emotions were more prevalent among people who felt increased stress during the day. A study of 100 nurses conscripted to treat COVID-19 patients in Wuhan, China, revealed that 45 percent experienced nightmares—twice the lifetime rate among Chinese psychiatric outpatients and many times higher than that among the 5 percent of the general population who have nightmare disorder.

It seems clear that some basic biological and social dynamics may have played a role in this unprecedented opening of the oneiric floodgates. At least three factors may have triggered or sustained the dream surge: disrupted sleep schedules augmenting the amount of rapid eye movement (REM) sleep and therefore dreaming; threats of contagion and social distancing taxing dreaming's capacity to regulate emotions; and social and mainstream media amplifying the public's reaction to the surge.

MORE REM SLEEP, MORE DREAMS

ONE OBVIOUS EXPLANATION for the surge is that sleep patterns changed abruptly when lockdowns took effect. Early publications demonstrate elevated levels of insomnia in the Chinese population, especially among frontline workers. In contrast, stay-at-home orders, which removed long commutes to work, improved sleep for many people. Chinese respondents reported an average increase of 46 minutes in bed and an extra 34 minutes in total sleep time. Some 54 percent of people in Finland said they slept more after lockdown. Overall, from March 13 to 27, 2020, time asleep in the U.S. increased almost 20 percent nationwide, and states with the longest commute times, such as Maryland and New Jersey, showed the largest increases.

Longer slumber leads to more dreams; people in sleep laboratories who are allowed to snooze for more than 9.5 hours recall more dreams than when sleeping a typical eight hours. Sleeping longer also proportionally increases REM sleep, which is when the most vivid and emotional dreams occur.

Relaxed schedules may also have caused dreaming to occur later than usual in the morning, when REM sleep is more prevalent and intense and, thus, dreams are more bizarre. Dream tweets reflect these qualities: "*I was taking care of a newborn girl that had COVID… it was so vivid and real.*" Increased dreaming during late-morning REM intervals results from the convergence of several processes. Sleep itself cycles through deep and light stages about every 90 minutes, but pressure for REM sleep gradually increases as the need for deep, recuperative sleep is progressively satisfied. Meanwhile a circadian process that is tightly linked to our 24-hour core body temperature rhythm gives an abrupt boost to REM sleep propensity late in the sleep period and stays elevated through the morning.

After the pandemic began, many people did sleep longer and later. In China, average weekly bedtime was delayed by 26 minutes but wake-up time by 72 minutes. These values were 41 and 73 minutes in Italy and 30 and 42 minutes among U.S. university students. And without commutes, many people were freer to linger in bed, remembering their dreams. Some early birds may have turned into night owls, who typically have more REM sleep and more frequent nightmares. And as people eliminated whatever sleep debts they may have accrued over days or even weeks of insufficient rest, they were more likely to wake up at night and remember more dreams.

DREAM FUNCTIONS OVERWHELMED

THE SUBJECT MATTER of many COVID-19 dreams directly or metaphorically reflects fears about contagion and the challenges of social distancing. Even in normal times, we dream more about novel experiences. For instance, people enrolled in programs to rapidly learn French dream more about French. Replaying fragments of experiences is one example of a functional role that researchers widely ascribe to REM sleep and dreaming: it helps us solve problems. Other roles include consolidating the prior day's events into longer-lasting memories, fitting those events into an ongoing narrative of our lives and helping us regulate emotions.

Researchers have documented countless cases of dreams assisting in creative achievement. Empirical studies also show that REM sleep aids in problem-solving that requires access to wide-ranging memory associations, which may explain why so many dreams in the 2020 surge involve creative or strange attempts to deal with a COVID-19 problem. One survey respondent said, "*I was looking for a kind of cream that would either prevent or cure Covid-19. I got my hands on the last bottle.*"

Two other widely claimed dream functions are extinguishing fearful memories and simulating social situations. They are related to emotion regulation and help to explain why pandemic threats and social distancing challenges appear so often in surge dreams. Many dreams reported in the media include fearful reactions to infection, finances and social distancing: "*I tested positive for pregnancy and covid … now I'm stressed.*" Threats may take the form of metaphoric imagery such as tsunamis or aliens; zombies are common. Images of insects, spiders and other small creatures are also widely represented: "*My foot was covered in ants and 5-6 black widows were imbedded in the bottom of my foot.*"

One way to understand direct and metaphoric imagery is to consider that dreams express an individual's core concerns, drawing on memories that are similar in emotional tone but different in subject matter. This contextualization is clear in post-traumatic nightmares, in which a person's reaction to a trauma, such as terror during an assault, is depicted as terror in the face of, for example, a natural disaster such as a tsunami. The late Ernest Hartmann, a Boston-area dream and nightmare research pioneer who studied dreams after the 9/11 attacks, stipulated that such contextualization best helps people adapt when it weaves together old and new experiences. Successful integration produces a more stable memory system that is resilient to future traumas.

Metaphoric images can be part of a constructive effort to make sense of disruptive events. A related process is the extinguishing of fear by the creation of new "safety memories." These possibilities, which I and others have investigated, reflect the fact that memories of fearful events are almost never replayed in their entirety during dreaming. Instead elements of a memory appear piecemeal, as if the original memory has been reduced to basic units. These elements recombine with newer memories and cognitions to create contexts in which metaphors and other unusual juxtapositions of imagery seem incongruous or incompatible with waking life—and, more important, are incompatible with feelings of fear. This creative dreaming produces safety imagery that supersedes and inhibits the original fear memory, helping to assuage distress over time.

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This mechanism can break down after severe trauma, however. When this happens, nightmares arise in which the fearful memory is replayed realistically; the creative recombining of memory elements is thwarted. The pandemic's ultimate impact on a person's dreams will vary with whether or how severely they are traumatized and how resilient they are.

A second class of theories—also still speculative—may explain social distancing themes, which permeated IDreamofCovid.com reports. Emotions in these dreams range from surprise to discomfort to stress to nightmarish horror. Tweets located by the @CovidDreams account illustrate how incompatible dream scenarios are with social distancing—so incompatible that they often trigger a rare moment of self-awareness and awakening: "*We were celebrating something by having a party. And I woke myself up because something wasn't right because we're social distancing and not supposed to be having parties.*"

These theories focus on dreaming's social simulation function. The view that dreaming is a neural simulation of reality, analogous to virtual reality, is now widely accepted, and the notion that the simulation of social life is an essential biological function is emerging. In 2000 Anne Germain, now CEO of sleep medicine start-up Noctem, and I proposed that images of characters interacting with the self in dreams could be basic to how dreaming evolved, reflecting attachment relationships essential to the survival of prehistoric groups. The strong interpersonal bonds reiterated during dreaming contribute to stronger group structures that help to organize defenses against predators and cooperation in problem-solving. Such dreams would still have adaptive value today because family and group cohesion remain essential to health and survival. It may be the case that an individual's concerns about other people are fine-tuned while they are in the simulated presence of those people. Important social relationships and conflicts are portrayed realistically during dreaming.

Other investigators, such as cognitive neuroscientist Antti Revonsuo of the University of Turku in Finland and the University of Skövde in Sweden, have since proposed additional social functions for dreaming: facilitating social perception (who is around me?), social mind reading (what are they thinking?) and the practice of social bonding skills. Another theory advanced by psychology professor Mark Blagrove of Swansea University in Wales further postulates that by sharing dreams, people enhance empathy toward others. The range of dream functions is likely to keep expanding as we learn more about the brain circuits underlying social cognition and the roles REM sleep plays in memory for emotional stimuli, human faces and reactions to social exclusion. Because social distancing is, in effect, an experiment in social isolation at a level never before seen—and is likely antagonistic to human evolution—a clash with deep-rooted dream mechanisms should be evident on a massive scale. And because social distancing disrupts normal relationships so profoundly—causing many of us to spend excessive time with some people and no time with others—social simulations in dreams may play a crucial role in helping families, groups, even societies deal with sudden, widespread social adaptation.

THE ECHO CHAMBER OF SOCIAL MEDIA

THERE IS ONE BASIC QUESTION about pandemic dreams that we would like to nail down: whether the dream surge was amplified by the media. It is quite possible that early posts of a few dreams were circulated widely online, feeding a pandemic-dreams narrative that went viral, influencing people to recall their dreams, notice COVID themes and share them. This narrative may have even induced people to dream more about the pandemic.

Evidence suggests that mainstream media reporting probably did not trigger the surge but may have temporarily amplified its scope. The Bulkeley and Solomonova-Robillard polls corroborated a clear groundswell in dream tweeting during March 2020, before the first media stories about such dreams appeared; indeed, the earliest stories cited various tweet threads as their sources.

Once stories emerged, more surges in dream reporting through early April 2020 were detected by IDreamofCovid.com and @CovidDreams. The format of most early stories almost guaranteed amplification: they typically described some salient dream themes observed in a survey and provided a link directing readers to participate in the same survey. In addition, 56 percent of articles during the first week of stories featured interviews with the same Harvard dream scientist, which may have influenced readers to dream about themes repeated by her.

The surge began to decline steadily in late April 2020, as did the number of mainstream media articles, suggesting that any echo-chamber effect had run its course. The final nature of the surge remains to be seen. Until COVID-19 vaccines or treatments are fully distributed and with waves of future infections or new viral variants possible, threats of disease and social distancing are likely to persist. Might the pandemic have produced a lasting increase in humanity's recall of dreams? Could pandemic concerns become permanently woven into dream content? And if so, will such alterations help or hinder people's long-term adjustments to our postpandemic futures?

Therapists may need to step in to help certain people. The survey information considered in this article does not delve into nightmares in detail. But some health-care workers who saw relentless suffering later themselves suffered with recurrent nightmares. And some patients who endured the ICU for days or weeks suffered from horrific nightmares during that time, which may in part have been the result of medications and sleep deprivation induced by around-the-clock hospital procedures and interminable monitor noises and alarms. These survivors will need expert help to regain normal sleep. Thankfully, specialized techniques are highly effective.

People who are not traumatized but still a little freaked out about their COVID dreams also have options. New technologies such as targeted memory reactivation are providing individuals with more control over their dream narratives. For example, learning how to practice lucid dreaming—becoming aware that you are dreaming—aided by targeted memory reactivation or other methods could help transform worrisome pandemic dreams into more pleasant, maybe even useful, dreams. Simply observing and reporting pandemic dreams seems to positively impact mental health, as Natália Mota of the Federal University of Rio Grande do Norte in Natal, Brazil, found in her studies.

Short of therapy, we can give ourselves permission to ease up and to enjoy banking those surplus hours of sleep. Dreams can be vexing, but they are also impressionable, malleable and at times inspirational. SA

Tore Nielsen is a professor of psychiatry at the Université de Montréal and director of the Dream and Nightmare Laboratory there.

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COPING WITH PANDEMIC STRESS

The COVID crisis has taken a terrible mental health toll. Coping methods based in disaster and trauma psychology can help

By Melinda Wenner Moyer

Illustrations by Cat O'Neil

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AMY NITZA HAS SPENT DECADES HELPING PEOPLE IN CRISIS. THE director of the Institute for Disaster Mental Health at the State University of New York at New Paltz has traveled to Puerto Rico in the wake of Hurricane Maria, to Botswana during an HIV crisis and to Haiti to help traumatized children forced into domestic servitude.

But the COVID-19 pandemic, Nitza says, is different. It keeps coming at people month after month as loved ones get sick or die, as jobs are lost, and as the actions taken to avoid infection—such as isolation from family—cause intense emotional pain and stress. Millions of people around the globe have died from the coronavirus, and the numbers keep climbing; grief, fear and economic hardship have hit every nation. The U.S. has the highest death toll on the planet—more than 550,000 people had perished by early April 2021—and millions on millions have become seriously sick. Usually disasters have survivors and responders, Nitza says, but COVID is so widespread that people are both of those things at once. "We're training everybody [on] how to take care of themselves and how to support the people around them," she says.

So far 2021 has been especially dark and hard. Deaths climbed to exceed the losses of 9/11 every day. Sometimes outbreaks recede but then rise back up again like storm-tossed seas. Millions of Americans still have not been vaccinated. Many hospitals are overwhelmed with waves of new COVID patients. So no one knows when the pandemic will end or whether the future will look anything like the past. "We as a nation have never been in anything like this," says Charles Figley, who has worked in disaster psychology for 40 years and is director of the Traumatology Institute at Tulane University in New Orleans.

The stresses are taking a terrible toll on our country's mental health. In June 2020 researchers at the Centers for Disease Control and Prevention surveyed 5,412 U.S. adults and found that 25.5 percent had symptoms of anxiety and 24.3 percent had symptoms of depression—a threefold and fourfold increase, respectively, from 2019. It is "a staggering number," says Susan Borja, chief of the National Institute of Mental Health's Dimensional Traumatic Stress Research Program. In a study that has not yet been peer-reviewed, researchers at the City University of New York and the University of North Carolina at Chapel Hill surveyed 5,250 U.S. adults in April 2020 and found that 35 percent had moderate or severe anxiety symptoms. Those who had recently lost income were doing extremely poorly.

The pains of the pandemic and its consequences are sharpest among people of color, who are "more exposed and less protected," in the words of physician Camara Phyllis Jones, who studies health inequities. In November 2020 unemployment rates among Black and Hispanic workers were 75 and 42 percent higher, respectively, than that among white workers. Compared with white households, many more Black and Hispanic households are struggling with food insecurity, and nonwhite children are more likely to be learning remotely from home rather than in person at school. These hardships fall on top of the direct agonies inflicted by the disease: In a study published in July 2020, New York University researchers found that in urban U.S. counties where the population was substantially nonwhite, the COVID death rate was nearly 10 times higher than it was in predominantly white counties with the same median income. Among Native Americans,

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another less protected group, the death rate during the first half of 2020 was nearly twice that among white people.

We can now glimpse, with the advent of vaccines, a time in the future when the pandemic sputters out. But to get there, we have to keep going through months of trauma and strain. How do we do that? How do we endure more and more of the isolation, the deaths, the flare-ups, the economic wreckage, the fear and the uncertainty?

There are ways—not perfect solutions but methods that can help. Psychologists who specialize in trauma and disaster recovery, as well as those who work with patients who have chronic injuries or disabilities, say that although it feels impossible and although there will be losses, most of us will get through this disaster. And they point to strategies for coping born of experience and science. When people in devastating situations can spot warning signs of mental trouble, acknowledge and express their distress, focus on the present moment and the small things they can control, and find ways to connect with others, they can get through the darkest of moments and show resilience.

"The majority of people who have a major catastrophic life event are going to eventually either return to baseline or, in some cases, come out better on the other side than they were before," says Megan Hosey, a rehabilitation psychologist at Johns Hopkins Medicine, who works with chronically ill patients in intensive care units. Most of us, she says, "will be able to adapt and recover." To do so, however, we will need to be flexible, open and honest with ourselves and learn how to take things one day at a time.

LOOK FOR WARNING SIGNS

IT CAN BE HARD TO TELL the difference, in the midst of a crisis, between normal levels of angst and those that indicate we might be edging into serious psychological problems. Key signs of declining mental health include changes in appetite or sleep patterns that last more than a week. If you find yourself becoming more irritable—maybe you are lashing out more frequently at your family members—that can be another sign of depression or anxiety. Having more trouble concentrating than usual or being unable to enjoy things you used to enjoy may also indicate that your mental health is declining and that you need to try new coping strategies.

Keep track, too, of how much you rely on medications, as well as on recreational drugs or alcohol. "We are seeing an uptick in substance and alcohol use in the context of the pandemic," Hosey says. This does not mean that it is dangerous to have a beer or a glass of wine when you are feeling stressed. But "if a medication or a substance is one of your primary ways of coping and you're finding you need more and more of it to get through the day, that's a red flag," she says.

Other things to look out for are physical symptoms such as pain, dizziness or indigestion. When people struggle emotionally, their distress often manifests itself physically (of course, serious physical symptoms warrant a visit to a physician to rule out other causes). Psychologist Tracy A. Prout and her colleagues at Yeshiva University, along with researchers at the University of Haifa in Israel and the University of Pisa in Italy, surveyed 2,787 adults around the world about their mental health during the pandemic. They found that the people who were experiencing the most distress also had the most physical symptoms, as the group reported in its study, published in November 2020 in *Frontiers in Psychology*.

FEAR IS OKAY

BEHIND THESE SIGNALS are the loneliness, unpredictability, fear and deprivation of the pandemic, and those are experiences that hospital patients with long-term illnesses and injuries know all too well. Mana Ali, a rehabilitation psychologist at MedStar National Rehabilitation Hospital in Washington, D.C., treats people with spinal cord injuries and paralysis. She says that one of the first things she tells these individuals is to acknowledge such emotions and to not feel bad about having them. "I always tell my patients, 'It's totally normal that the anxiety is there—it's about managing it,'" she says. We tend to think that fear and worrying are bad and that strength is the absence of those things, but that is not the case, she adds: "You can feel scared and fearful and angry and resentful and simultaneously be a victor and be resilient. Reminding people that they are both, versus either/or, is extremely important."

> "You can feel scared and fearful and angry and resentful and simultaneously be a victor and resilient. Reminding people that they are both is extremely important."
> —Mana Ali, psychologist *MedStar National Rehabilitation Hospital*

Disaster and rehabilitation psychologists have done research showing that writing about negative feelings is very effective. "There's something about writing it down that's super important," Nitza says. In the early 1980s psychologist James W. Pennebaker, then at the University of Virginia, and his colleague conducted a study in which they told some college students to write about their stressful experiences and feelings for 15 minutes a day four days a week. They told others not to do anything unusual. The students who engaged in this "expressive writing," as Pennebaker called it, were only half as likely to visit the student health center over the next six months as those who did not. More recent analyses have supported these findings, confirming that writing about feelings is a powerful way to work through them.

These admissions about negative emotions are important because they "open the door for, 'What can I do next?'" Hosey explains. To be fair, this question can be hard to answer in the midst of a world-shaking pandemic. Nitza suggests trying to pinpoint what exactly worries you most at the moment and then identifying aspects of the situation that you can control or make progress on. If you have just lost your job and you are worried about paying your bills, brainstorm small things you can do to give yourself a sense of control. Maybe a goal for this week is to create a new household budget or to find out about financial relief programs you might be eligible for.

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This kind of brainstorming requires open-mindedness about "things you're willing to learn and try," explains Deepa Ramanathan-Elion, a rehabilitation psychologist at the National Intrepid Center of Excellence at Fort Belvoir in Virginia, who works with military service members who have traumatic brain injuries. "If you continue in a sort of rigid way of thinking, it's going to be very difficult for you to adapt to a changing environment, no matter what the situation is—whether it's COVID or something else," she says. "You really need to be able to adapt and be flexible." That might mean considering jobs you would not have considered in the past or asking people you would not normally reach out to for help or support.

The idea is to think of problems as obstacles you can overcome (at least partially) rather than as insurmountable hurdles you can do nothing about. There are aspects of this pandemic we cannot control—but by focusing on the things we can tweak at least a bit and by thinking of ourselves as resilient and adaptable, we will do better, Ali says. Cognitive-behavioral therapy, which focuses on helping individuals identify, understand and change their thinking and behavior patterns in these ways, has consistently been shown to boost mental health. A 2020 study found that Internet-based cognitive-behavioral therapy improved symptoms in people suffering from either anxiety or depression.

Ali often thinks of her father and his family, who are from Somalia and have faced many hardships. "They have absolutely nothing, but they have this strong sense of resilience," she says. "If they feel like they can get through it, they can get through it. So trying to cultivate that in people, regardless of resources—having them see that 'you can do this'—I think is very, very, very important."

FIND NEW WAYS TO CONNECT

SEEKING OUT OTHERS can help, too. Researchers at the RAND Corporation found, based on interviews done after the 9/11 terrorist attacks, that the most common way adults dealt with their distress was by connecting with friends and family.

The trouble now is that staying safe during this pandemic strains those connections. It often requires physical distance from loved ones, which means people are forced to give up what they emotionally need the most. In a 2015 analysis of 70 studies, researchers at Brigham Young University found that people who reported feeling lonely were 26 percent more likely to die over the next seven years, on average, than those who were not lonely. "There is a consistent and growing—and highly replicated across context and across countries—literature on the detrimental effects of social isolation and loneliness and the mitigating or positive well-being effects of social support," says Courtney Welton-Mitchell, a psychologist at the Colorado School of Public Health and at the Natural Hazards Center at the University of Colorado Boulder. (If you are feeling extremely isolated or are having thoughts of suicide, please call the National Suicide Prevention Lifeline at 1-800-273-8255.)

If you are older and alone, connecting with others can be hard, especially if you are not tech-savvy enough to link up over a computer or a smartphone. Welton-Mitchell suggests reaching out to family members and friends regularly by phone, e-mail or snail mail and perhaps setting up regular phone calls or physically distanced visits. You can also sign up for Caring Calls, a service organized by the nonprofit organization DOROT, which facilitates once- or twice-weekly telephone conversations between older adults and volunteers. To sign up by phone, call 1-212-769-2850. If you are comfortable using the Internet, you can sign up for a service such as Big & Mini or Eldera, either of which connects older adults with younger people through video calls.

If you are older and alone, connecting with others can be hard, especially if you are not tech-savvy. You can sign up for Caring Calls, which facilitates weekly phone conversations between older adults and volunteers.

Working toward a meaningful cause—even from the safety of your home—can also improve emotional health. It helps to "feel like you're committing to something that's greater than yourself," says William Garmoe, a neuropsychologist who works with Ali at MedStar National Rehabilitation Hospital. In a 2007 paper, a group of 20 international disaster psychologists analyzed research on the most important psychological needs people have in the midst of a disaster. They reported the top five are to feel safe, calm, self-efficacious, socially connected and hopeful. When people engage in activities that benefit others, they may be able to check off three of those needs—feeling more useful, connected and hopeful about the future. If you are not sure where to start, search VolunteerMatch.org or Idealist.org for local or virtual opportunities.

Virtual therapy provides another means of connection. Since the pandemic began, federal and state legislation has loosened a number of restrictions on the use of telemedicine, so it is now easier for people to access mental health services online. Finding a therapist can be difficult if you do not have health insurance or the means to pay, but free or low-cost options do exist: Opencounseling.com, for instance, allows you to search for free or low-cost therapists in addition to those who accept insurance or who can be paid for out of pocket.

One key benefit of therapy is the close relationship between the patient and the provider, which fosters a strong sense of belonging. "You're meeting with somebody with whom you have a real relationship—this is a person who cares about you, seeks to understand you, is warm and accepting," says Bruce Wampold, a professor emeritus of counseling psychology at the University of Wisconsin–Madison. "And for many people, this is particularly healing."

Therapy can also help by nudging people toward constructive ways of coping with stress and anxiety. In their November 2020 study, Prout and her colleagues surveyed adults about what strategies they used to make themselves feel better during the pandemic. They found that people who connected with and

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helped others felt less distressed than those who coped in less healthy ways, such as by repressing their feelings or expressing hostility indirectly.

PAY ATTENTION TO YOURSELF

ONE OF THE HARDEST THINGS about the coronavirus is that it creates so much uncertainty about the future. "We like to be able to plan and set goals," Ramanathan-Elion says. "We like to go through life in this very organized fashion." Yet many of us do not know when we will get access to a COVID vaccine or whether we can pay next month's rent or when social isolation will end. We do not know whether we will get sick with COVID or what will happen if we do.

Psychologists who work with those who have serious injuries or chronic illnesses note that such people always have to manage an unknown future, and they often do so best by focusing on the present—paying attention to their sensations and feelings in the moment rather than focusing on what cannot be known with any assurance. The goal is to "just look at this one day at a time. Because we really don't know what tomorrow is going to look like," Hosey says.

One evidence-based approach that helps people stay grounded in the present is "mindfulness," and there are various ways to do it, including through short meditations. A 2018 review and analysis of 18 studies concluded that regular mindfulness exercises—such as focused breathing and "body scans," in which you pay attention to how the parts of your body feel and try to relax them—reduce symptoms of anxiety and depression even in the absence of any other treatments. (If you want to try guided meditations, Ramanathan-Elion recommends the smartphone apps Breathe2Relax and Mindfulness Coach.)

If the idea of meditation makes you uncomfortable, it is possible to be mindful without it. One way is to focus on the sensations you experience while you do everyday things such as eating and brushing your teeth. Nitza says she recently bought several adult coloring books because she has found that coloring is what helps her "focus my attention on the immediate thing."

However we get to it, mindfulness makes us feel calmer because "it slows down our breathing, and it sends that message to the brain that we're okay and there's no trigger in the environment; there's no stressful issue that we need to be attending to," Ramanathan-Elion says.

There is no one-size-fits-all approach to keeping your mental health intact, and the approach that is best for you will depend on your situation, your access to resources and your preferences. Psychologists say to trust your instincts and to try the available strategies that you think might help the most. Be willing to try out new things if the approaches you first choose do not seem to be working.

And keep in mind that the more time we spend in this pandemic, the better we will get at muddling our way through—because people adapt surprisingly well to challenging situations. It has been tough, and it could get tougher, no question. But humans are "stronger than they think," Figley says. "I frequently find that people are unbelievably resilient." SA

Melinda Wenner Moyer, a contributing editor at *Scientific American*, is author of the forthcoming book *How to Raise Kids Who Aren't Assholes: Science-Based Strategies for Better Parenting—from Tots to Teens* (G. P. Putnam's Sons, July 2021).

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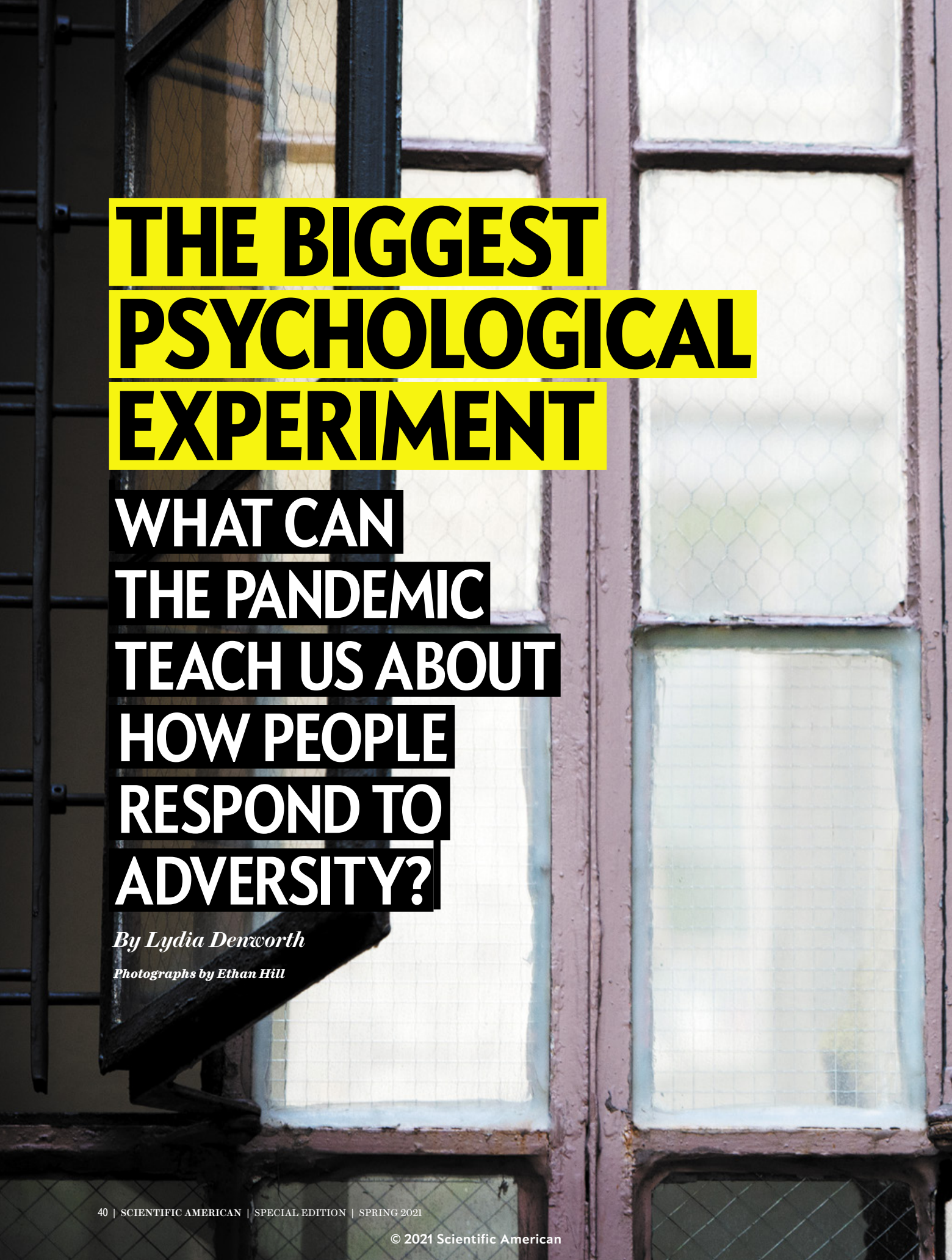

THE BIGGEST PSYCHOLOGICAL EXPERIMENT

WHAT CAN THE PANDEMIC TEACH US ABOUT HOW PEOPLE RESPOND TO ADVERSITY?

By Lydia Denworth

Photographs by Ethan Hill

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BERNELL GRIER, who leads a community development corporation in Brooklyn, N.Y., is helping Black people affected by the pandemic.

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THE IMPACT OF COVID-19 ON THE PHYSICAL HEALTH OF THE WORLD'S CITIZENS HAS BEEN extraordinary. By April 2021 there were almost 130 million cases spread across more than 190 countries. The pandemic's effect on mental health could be even more far-reaching. At one point roughly one third of the planet's population was under orders to stay home. That means 2.6 billion people—more than were alive during World War II—were experiencing the emotional and financial reverberations of this new coronavirus. "[The lockdown] is arguably the largest psychological experiment ever conducted," wrote health psychologist Elke Van Hoof of Free University of Brussels-VUB in Belgium. The results of this unwitting experiment are only beginning to be calculated.

The science of resilience, which investigates how people weather adversity, offers some clues. A resilient individual, wrote Harvard University psychiatrist George Vaillant, resembles a twig with a fresh, green living core. "When twisted out of shape, such a twig bends, but it does not break; instead it springs back and continues growing." The metaphor describes a surprising number of people: As many as two thirds of individuals recover from difficult experiences without prolonged psychological effects, even when they have lived through events such as violent crime or being a prisoner of war. Some even go on to grow and learn from what happened to them. But the other third suffers real psychological distress—some people for a few months, others for years.

Even if most individuals prove resilient, the toll of the COVID-19 disruptions and the sheer numbers involved have experts warning of a mental illness "tsunami." People face a multiple wallop: the threat of disease, loneliness of isolation, loss of loved ones, repercussions of job loss and ongoing uncertainty about when the pandemic will end. Depression, anxiety and post-traumatic stress will undoubtedly follow for some. Mental health hotlines have reported surges in calls, and early surveys found high levels of concern. "This pandemic just ticks all the boxes in terms of the kinds of stressors that are going to be difficult," says psychologist Anita DeLongis of the University of British Columbia, who studies psychosocial responses to disease. The deaths by suicide of health care professionals who had been on the medical front lines are powerful reminders of the risks.

Individual resilience is further complicated by the fact that this pandemic has not affected each person in the same way. For all that is shared—the coronavirus has struck every level of society and left few lives unchanged—there has been tremendous variation in the disruption and devastation experienced. Consider Brooklyn, just one borough in hard-hit New York City. Residents who started 2020 living or working within a few miles of one another have very different stories of illness, loss and navigating the challenges of social distancing. How quickly and how well individuals, businesses and organizations recover will depend on the jobs, insurance and health they had when this started, on whether they have endured hassle or heartbreak, and on whether they can tap financial resources and social support.

The pandemic has laid bare the inequities in the American health care system and economic safety net. Black and Latino Americans are dying at much higher rates than white Americans. "When we talk about preexisting conditions, it isn't just if I'm obese; it's our society's preexisting condition," says medical anthropologist Carol Worthman of Emory University, an expert in global mental health.

Fortunately, the unprecedented pandemic is leading to unprecedented science not just in virology but on mental health and resilience. Behavioral scientists are measuring the psychological toll in real time and striving to identify what helps people cope. Unlike, say, the September 11 terrorist attacks or Hurricane Katrina, which occurred over a finite period even though their effects were drawn out, the open-ended time frame for COVID allows for new kinds of longitudinal studies and research directions. The sudden mass switch to virtual forms of working and socializing is expected to jump-start more nuanced investigations into what makes social interaction satisfying—or stultifying. If

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WHEN TOM INCK (*top right*) **fell ill with COVID-19, his wife, Wendy Blattner** (*standing*)**, cared for him while managing upheavals in her business and their daughters' lives.**

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researchers meet the challenge of COVID, says psychiatrist Dennis Charney of the Icahn School of Medicine at Mount Sinai, "there will be a whole new science of resilience. We could learn how to help people become more resilient *before* these things happen."

BEND BUT DON'T BREAK

RAFAEL HASID ARRIVED in New York City from his native Israel in 2000 to attend the French Culinary Institute. In 2005 he opened a restaurant called Miriam in Brooklyn that became a neighborhood favorite. In the first weeks of March 2020, Hasid could see what was coming. "I was following the news in Israel," he says. "We were two weeks behind in every respect. I was saying, 'This is going to happen here.'" When Miriam's popular weekend brunch attracted a third of the usual crowd, Hasid did not spend much time wondering what to do: he gave away all of the restaurant's perishable food to the neighbors. By the time the city required all restaurants to shut down, Miriam had already closed.

EVEN IF MOST INDIVIDUALS PROVE RESILIENT, THE TOLL OF THE COVID-19 DISRUPTIONS AND THE SHEER NUMBERS INVOLVED HAVE EXPERTS WARNING OF A MENTAL ILLNESS "TSUNAMI."

Faced with potentially traumatic events, "about 65 percent of people are going to show minimal psychological symptoms," says clinical psychologist George Bonanno of Teachers College at Columbia University. Bonanno, who is an expert on resiliency, studies the aftermath of hurricanes, terrorist attacks, life-threatening injuries and epidemics such as the 2003 SARS outbreak. His research and that of others consistently shows three common psychological responses to hardship. Two thirds of people follow a resilience trajectory and maintain relatively stable psychological and physical health. About 25 percent struggle temporarily with psychopathology such as depression or posttraumatic stress disorder and then recover—a pattern known as the recovery trajectory. And 10 percent suffer lasting psychological distress. These results hold true across diverse populations and socioeconomic statuses. "We're talking about everybody," Bonanno says. On the other hand, the risk of psychiatric disorders is twice as high for people on the lowest economic rungs.

But the mental health effects of a crisis so sweeping and insidious may not adhere to this paradigm. Studies show that strict quarantine can lead to negative psychological effects such as PTSD, although few of us have been under true quarantine, which refers to isolating after a possible exposure to infection. Instead much of the world is living with restrictions that Bonanno suspects amount to something more like managing constant stress. "This is the first time in living history we've had a global lockdown that's gone on for such a long time," says epidemiologist Daisy Fancourt of University College London. "We simply don't know how people are going to react to this."

The potential scope of the impact is considerable. "This is different from other forms of stress because it's not just one domain of your life," says health psychologist Nancy Sin of the University of British Columbia. "People are dealing with relationship or family challenges, with financial and work challenges, with health."

Early reports were showing clear effects. The first nationwide large-scale survey in China, where the crisis hit earliest, found that almost 35 percent reported psychological distress. In the U.S., rising fear and anxiety about COVID have been found in people who already suffer from anxiety. Another study captured worrisome findings in older adults. This is surprising because previous research shows that, for the most part, older adults have better emotional well-being. "During this pandemic, older adults don't have those age-related strengths in emotions that we would typically expect," says Sin, who studies aging and is collaborating with DeLongis in an ongoing COVID-19 study of 64,000 individuals worldwide. "They are reporting just as much stress as middle-aged and younger people."

Sin is still analyzing the causes of the stress but suspects it is caused by older adults' higher likelihood of getting sick and of losing loved ones. Older people are coping with their stress better than younger people, however, and reporting less depression or anxiety. They may be benefiting from the perspective that comes with having lived through more than younger people, Sin says. Adults older than 65 have also had more time to develop skills for dealing with stress, and many have retired and so are less likely to be concerned about work.

Fancourt began a study in mid-March 2020 that at one point grew to include more than 90,000 U.K. residents. It is tracking depression, anxiety, stress and loneliness week by week. "We need to know in real time what's happening," Fancourt says. Six weeks in, they found that levels of depression were significantly higher than before the pandemic.

Generally, those with previously diagnosed mental health illnesses, those who live alone and younger people were reporting the highest levels of depression and anxiety. On the positive side, there was a slight decrease in anxiety levels once the lockdown was declared. "Uncertainty tends to make things worse," Fancourt says. Some are frozen by not knowing what is to come, whereas others find ways to carry on.

After Hasid's restaurant had been closed for three weeks, he had not yet received any of the government payments meant to protect small businesses. While his situation was rife with uncertainty, "I was thinking that we have to continue creating business for ourselves," he says. When a few customers e-mailed to inquire if

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he would consider catering their Passover seders, Hasid developed a prix fixe holiday menu for delivery. Before the pandemic, Hasid was planning to open a delicatessen that would be located in an adjacent storefront. Instead of renovating the new space, he opened the deli inside the restaurant. His biggest worry was whether employees would feel safe. To reassure them, in addition to social distancing, he requires masks and gloves and has someone come in to bleach the restaurant morning and night. Hasid also looked into other sanitizing strategies involving blowers and alcohol that he heard had been used in Singapore.

Hasid recognizes that his ability to adapt is not something every business can do, especially many restaurants that run on tight margins. The new operation used minimal staff, but Hasid continued to pay—out of his own pocket—any employees who were not able to get through to unemployment. Serving food via delivery brings in less than a third of Miriam's former income, but he says it is better than nothing. Last year the restaurant also began preparing a weekly meal for a local hospital. "It is not a money maker, but it's the least we can do." Hasid is pleased with Miriam's reinvention and optimistic that the restaurant will ultimately survive. "We are in a much better situation than a lot of other places in New York," he says.

THE COMPONENTS OF COPING

WHEN BROOKLYN RESIDENT TOM INCK developed a persistent fever and dry cough in the middle of March 2020, the psychotherapist and management consultant feared he had COVID. Because of the shortage of tests at the time, Inck's doctor first screened for every other known virus (Inck paid for the test panel). Then doctor and patient met on the streets of Manhattan. Standing on Madison Avenue in full protective equipment, the doctor administered the test, which came back positive six days later.

Successfully coping in a crisis means continuing to function and engaging in day-to-day activities. One must solve problems (whether that means getting groceries or a virus test), regulate emotions and manage relationships. There are factors that predict resilience such as optimism, the ability to keep perspective, strong social support and flexible thinking. People who believe they can cope do, in fact, tend to cope better.

During nine days of isolation in a spare room, Inck filled the time with meditating and reading. In some ways, things were harder for his wife, Wendy Blattner, who was managing her husband's care, the transition of her marketing agency to remote work, and the emotions of the couple's two college-aged daughters, who were upset at the loss of their semesters and anxious about their father. Blattner left meals outside her husband's door and got up every three hours throughout the night to record his temperature and blood oxygen level. She was scared but resolute. "I felt like he had excellent care, even though it was remote, and that I had the resources within myself and the support I needed," she says. "That's what I told my kids and what I told myself—that it might get rough, but it was going to be okay."

Most people's coping skills can be strengthened. Several of the new studies are designed to identify successful strategies that buffer the effects of the stress. So far, Fancourt says, people are encouraged to follow classic mental health strategies: getting enough sleep, observing a routine, exercising, eating well and maintaining strong social connections. Spending time on projects, even small ones, that provide a sense of purpose helps.

In previous work, DeLongis has shown that those who are high in empathy are more likely to engage in appropriate health behaviors such as social distancing and to have better mental health outcomes than people who are low in empathy. But her earlier studies of diseases such as SARS and West Nile were cross-sectional and captured only a moment in time. Her COVID-19 study followed people's behavior and attitudes for months to capture changes in empathy and coping over time. "This isn't just about a trait of empathy," DeLongis says. Empathetic responses can be learned and encouraged with proper messaging, and her hunch was that increases or decreases in empathetic responding over weeks and months would be associated with shifts in health behaviors and coping mechanisms.

As part of DeLongis's study, Sin asked people to record their daily activities and emotions for a week. In the early months of the pandemic, she says, the picture was "that life is really challenging, but people are finding ways to meet that challenge." Many reported a great deal of positive social interactions, many of them remote. Older adults reported the highest levels of positive experiences in their daily lives, often through providing support to others.

It is striking that remote connections are proving satisfying. Previous research on the effects of digital technology and media focused on the association between time spent on screens and psychological well-being but revealed little about the worth of different kinds of online interaction. Now that the world is relying on the Internet to socialize, investigating those nuances is crucial. Should social media closely mimic face-to-face interaction, or can less intense forms of communication leave people feeling connected? We do not know yet, but it is likely those studies will now get funded when previously they weren't. "I think we just skipped a decade of conversation in a month," says psychologist Amy Orben of the University of Cambridge, who studies adolescent mental health and technology use.

Social media is a factor in other kinds of research as well. Psychologist Roxane Cohen Silver of the University of California, Irvine, is assessing the impact of media exposure on people's well-being. "Those who consume a great deal of news about a community-wide crisis are more distressed," she says. Computational social scientist Johannes Eichstaedt of Stanford University is combining large-scale analyses of Twitter with machine learning to capture levels of depression, loneliness and joy during the pandemic.

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RESTAURANT owner Rafael Hasid rapidly reinvented his business for take-out and delivery but was paying employees out of his own pocket.

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As Blattner feared, things did get rough for their family. On nights seven and eight, when Inck's fever hovered around 103 and his blood oxygen levels dropped to 93, his doctor (via Zoom) said if the levels stayed there or got worse, Inck should go to the hospital. "I'm not going to have a patient who dies at home," he said, a statement that alarmed the children. "The toughest thing for us was the fear," Inck says. But Tylenol kept the fever in check, and short, shallow breaths kept Inck's blood oxygen level in the safety zone. After 10 days, he began to feel better.

The experience left Inck grateful and energized. He threw himself back into work counseling others who were sick and signed up to be a plasma donor for critical patients. But, unlike others who recovered, he did not initially venture out much. "The world felt like a vulnerable place," he says.

SOCIETY'S PREEXISTING CONDITIONS

EVEN THOSE BRIMMING with personal resilience need outside help if they face challenges on multiple fronts. As executive director of IMPACCT Brooklyn, a community development corporation that serves the historically Black neighborhoods of Brooklyn, Bernell K. Grier sees just how hard the pandemic has hit the African-American community. "Daily, I'm hearing of people who are either COVID-positive, recovering from it or have died from it," she says. Three of those deaths occurred in apartments that Grier manages and required her to organize deep-cleaning services. Still, she pressed on. "Seniors are fearful of going out, fearful of anyone coming to their front door," Grier says. "They also are not tech-savvy. A lot of things where they're being told to go on the computer, they need someone to hold their hand and help them through the process."

The pandemic, Fancourt says, "is going to exacerbate the social gradient that we're used to seeing across society. It's crucial that [people] have interventions at a national level that can support [them]." In the U.K., such interventions include the National Health Service and a furlough program that pays up to 80 percent of the salaries of millions of Britons who could not work because of the pandemic. In the U.S., paycheck-protection packages and unemployment exist but proved difficult to access quickly.

Grier's organization provides a variety of services around housing, small business advocacy, and interaction with financial and government institutions. As soon as the pandemic hit, her staff distributed information about public health and economic resources. They introduced webinars to help businesses apply for loans. As of late April 2020, "none of the ones that we helped got anything," Grier says. "It's not reaching our businesses." Only 70 percent of Grier's tenants were able to pay rent in April 2020. "We still have to pay the supers, the porters, the heat and electricity, the taxes and everything else," Grier says. "It's a domino effect. If the residents can't pay, we can't pay."

Worthman, the Emory anthropologist, says the ability to cope with the pandemic's reverberations is not just an individual issue but a societal one. It is also an opportunity. "People have pointed to periods of disaster in American history, after World War I and the Depression, that led to real structural change that benefited people."

Grier is advocating for positive change for her community. In her talks with public health and elected officials, she points out disparities such as the fact that the first test centers were not located in poor neighborhoods. "This is a spotlight on what has existed for too long," she says. "When you're looking at [solutions], make sure that income equality and a racial-equity lens is a filter for everything that's put in place." As Brooklyn reemerges from social isolation, Grier knows the critical role groups like hers play. "We will continue to be here to be that liaison, that credit counselor, that navigator."

Cultivating resilience though community support appears to be more important than ever. As a school nurse in Brooklyn, Marilyn Howard, who immigrated from Guyana as a teenager, worked through the early weeks of March 2020 until the public schools closed. She got sick the day after she left work. It took 10 days to get the test results that confirmed she had COVID. By then Howard thought she was on the road to recovery. But on Saturday, April 4, she awoke with labored breathing that rapidly worsened. Her brother Nigel Howard, with whom she shared an apartment, called an ambulance. But April 4 was near the peak of the pandemic in Brooklyn, and there was no ambulance available. Nigel drove them to the nearest hospital, but Marilyn's breathing deteriorated on the way. Less than a minute before they arrived, her heart stopped, and she could not be revived. She was 53.

"A couple of simple things could have saved my sister's life," says Haslyn Howard, the youngest of Marilyn's five brothers. If schools had closed earlier or her colleague could have taken a sick day, she might not have gotten sick. If someone had recommended a pulse oximeter, she would have known to go to the hospital sooner. If an ambulance had been available.... The Howard brothers arranged a viewing at a Long Island funeral home to provide some closure. Haslyn permitted only three people in the room at a time, but a simultaneous virtual service allowed more than 250 people to celebrate Marilyn's life.

Nigel later tested positive for COVID and isolated at home. "My brothers and I are in the initial phases of trying to plan an organization that targets efforts to help the Black and brown community, poor communities, address some of these [issues] on a local and tangible level," Haslyn said soon after losing his sister. It is something they can do in her memory that would have made her proud. "That's one of the ways that we're coping," he adds. "How do we turn tragedy into triumph?" SA

Lydia Denworth is a Brooklyn, N.Y.–based science writer, a contributing editor for *Scientific American*, and author of *Friendship: The Evolution, Biology, and Extraordinary Power of Life's Fundamental Bond* (W. W. Norton, 2020).

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THE HEALTH-WEALTH GAP

The growing gulf between rich and poor inflicts biological damage on bodies and brains

By Robert M. Sapolsky

WESTERN CULTURES HAVE LONG CHERISHED THE NOTION that all people are created equal. But in the real world, our lives are not balanced with equal opportunities and resources. This distinction was noted mordantly in 1894 by author Anatole France, who wrote that "the law, in its majestic equality, forbids the rich as well as the poor to sleep under bridges, to beg in the streets, and to steal bread." The rich, of course, need none of these things, whereas the poor often have little choice. And economic disparity has only gotten worse during the past several decades, particularly in the U.S. In 1976 the richest 1 percent of U.S. citizens owned 9 percent of the country's wealth; today they own about 30 percent. This trend echoes around the globe.

One of the consequences for the growing poor is worsening health, and the reasons are not as obvious as you might think. Yes, lower socioeconomic status (SES) means less access to health care and living in more disease-prone neighborhoods. And, yes, as the SES ladder's lower rungs have become more populated, the number of people with medical problems has climbed. This is not merely an issue of poor health for the poor and some version of better health for everyone else. Starting with Jeff Bezos at the top, every step down the ladder is associated with worse health.

The link between socioeconomic inequality and poor health goes beyond simple access to care and living with more dangers. Less than half of the health changes along this SES/health ladder can be explained away by risks such as smoking, alcohol consumption and reliance on fast food or by protective factors such as insurance and health club memberships. In the U.K., large, long-term studies of risks in specific groups, led by epidemiologist Michael Marmot and called the Whitehall studies, demonstrated this clearly. Further, this ladder, or gradient, exists in nations with universal health care; if care availability were truly responsible, universal access should make the

Illustration by Andrea Ucini

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gradient vanish. Something else, something quite powerful, must be associated with inequities and be able to cause health problems.

That factor seems to be the stressful psychosocial consequences of low SES. Psychologist Nancy Adler of the University of California, San Francisco, and her colleagues have demonstrated that how people rate how they are doing, relative to others, is at least as predictive of health or illness as are any objective measures such as actual income level. The research indicates that poor health is as much about feeling poor as being poor. Epidemiologists Richard Wilkinson and Kate Pickett of the University of Nottingham and the University of York in England, respectively, have filled out this picture in detail, showing that while poverty is bad for your health, poverty amid plenty—inequality—can be worse by just about any measure: infant mortality, overall life expectancy, obesity, murder rates, and more. Health is particularly corroded by your nose constantly being rubbed in what you do not have.

Basically, more unequal societies have worse quality of life. Across countries and among U.S. states, more inequality, independent of absolute levels of income, predicts higher rates of crime, including homicide, and higher incarceration rates. Add in higher rates of kids being bullied at schools, more teen pregnancies and lower literacy. There are more psychiatric problems, alcoholism and drug abuse, as well as lower levels of happiness and less social mobility. And there is less social support—a steep hierarchy is the antithesis of the equality and symmetry that nourish friendship. This grim collective picture helps to explain the immensely important fact that when inequality increases, everyone's health suffers.

This is where the problem affects the rich, the haves, as well as the have-nots. With increasing inequality, they typically expend more resources insulating themselves from the world underneath the bridges. I have heard economist Robert Evans of the University of British Columbia call this the "secession of the wealthy." They spend more of their own resources on gated communities, private schools, bottled water and expensive organic food. And they give lots of money to politicians who help them maintain their status. It is stressful to construct thick walls to keep everything stressful out.

Knowing that these psychological and social factors influence the biology of disease is one thing. Demonstrating just how these stressors do their dirty work inside the body is something else. How do SES and inequality "get under the skin"? It turns out that researchers have made significant strides toward an answer. We have learned a lot about how poverty affects biology, and the part of the growing inequality gap that worries people is the poverty end. Scientists have been able to trace physiological connections from external inequality to three key inner areas: chronic inflammation, chromosomal aging and brain function.

A HEAVY LOAD

THINKING ABOUT the biology of disease was revolutionized in the 1990s, when the late Bruce McEwen of the Rockefeller University introduced the concept of allostatic load. Our bodies are constantly challenged by our environment, and we stay healthy when we meet those challenges and return to a baseline state, or homeostasis. Traditionally this view led scientists to focus on specific organs that solve specific challenges. Allostasis has a different perspective: physiological challenges provoke far-flung adaptations throughout the body. An infected toe, for instance, will produce not only inflammation at the tip of the foot but also wider changes in everything from energy taken from abdominal fat to the brain chemistry of sleepiness. As this biological grind continues, it leads to an array of body parts functioning less than optimally, which can be as damaging to health as a single organ gone very wrong.

Teresa Seeman of the University of California, Los Angeles, took this idea and followed it through the body, measuring various biomarkers of wear and tear, including increases in blood pressure, cholesterol, blood lipids, body mass index, molecular indicators of chronic hyperglycemia, and levels of stress hormones. She showed that this group of disparate measures powerfully predicts physical health and mortality.

Recent research by Seeman and others links low SES with heavy allostatic load because the body is in a constant and futile battle to return to a normal, nonstressed state. These findings highlight an important theme: whereas an adult's SES predicts allostatic wear and tear, childhood SES leaves a stronger lifelong mark. Low SES predisposes youngsters' bodies toward earlier "aging." The scientists also found protective factors. Although growing up in an impoverished neighborhood worsens the low SES–allostatic load link, lucking out with a mother who has the time and energy to be highly nurturing reduces the ill effects.

Stress in any form can produce these effects. It does not have to be related to money, but it is usually related to social situations. My own work with baboons living freely on the East African savanna has shown this effect. In baboon groups, an animal's place in the social hierarchy produces more or less stress. If you are a low-ranking baboon—a socially stressful situation—your body has unhealthy abnormalities in its secretion of glucocorticoids, which are stress hormones such as cortisol. The body also shows unhealthy changes in the gonadal, cardiovascular and immune systems.

In animal and human hierarchies, these stress-induced changes affect health through a key process: chronic inflammation. Few things are better examples of a double-edged biological sword than inflammation. After tissue injury, inflammation contains damage and initiates cell repair. Chronic widespread inflammation, however, causes molecular damage throughout the body, and studies have demonstrated that it contributes to diseases ranging from atherosclerosis

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to Alzheimer's. Recent work (including my own focusing on inflammation of the nervous system) indicates that chronic high stress levels can promote chronic inflammation. In people, childhood poverty upregulates the adult body's proinflammatory set point, with increased expression of inflammatory genes and increased levels of inflammatory markers such as C-reactive protein, which is associated with a higher risk of heart attacks.

These are long-term effects: more financial losses in the Great Recession predict higher C-reactive protein levels six years later. Humans share such vulnerabilities with other primates that live in unequal circumstances. Work by Jenny Tung of Duke University shows more markers of chronic inflammation in low-ranking rhesus monkeys compared with the socially dominant animals in a group. Such studies highlight the directness of the link between social stress factors and unhealthy biology because that link occurs in a species that lacks changes in lifestyle risk factors, such as increased rates of smoking and drinking, that we often see in humans who are stuck in low-status situations.

PREMATURE DNA AGING

PROGRESS in understanding the routes into the body taken by the SES/health gradient has also come through a very sensitive measure of aging: the condition of telomeres, which are the stretches of DNA at the very tips of chromosomes.

Telomeres help to keep our chromosomes stable—molecular biologists like to say that they resemble the plastic caps at the ends of shoelaces that prevent fraying. Every time chromosomes are duplicated for cell division, the telomeres shorten; when they get too short, cells can no longer divide, and they lose many of their healthy functions. Telomere shortening is countered by the enzyme telomerase, which rebuilds these tips. Thus, the state of a cell's telomeres tells much about its biological "age," and shortened telomeres that produce frayed, vulnerable chromosomes seem to be a molecular version of wear and tear.

Telomere biology met stress physiology in a 2004 study by health psychologist Elissa Epel of U.C.S.F. and molecular biologist Elizabeth Blackburn of the Salk Institute for Biological Studies; Blackburn won the Nobel Prize for her pioneering work on telomeres. They examined 39 people who lived with severe stress every day: women who were caregivers for chronically ill children. The landmark finding was that white blood cells in these caregivers had shortened telomeres, decreased telomerase activity, and elevated oxidative damage to proteins and enzymes. (Oxidation can disable telomerase.) The longer a child's illness, the more stress the women reported and the shorter their telomeres

INSIDE INEQUALITY

Life in societies with wide gaps between rich and poor creates ongoing social and psychological stresses. These grind down the body in a host of unhealthy ways, affecting our brains, our immune systems and our DNA, according to a broad range of research. Here are some effects that can lead to serious physical illnesses and mental problems.

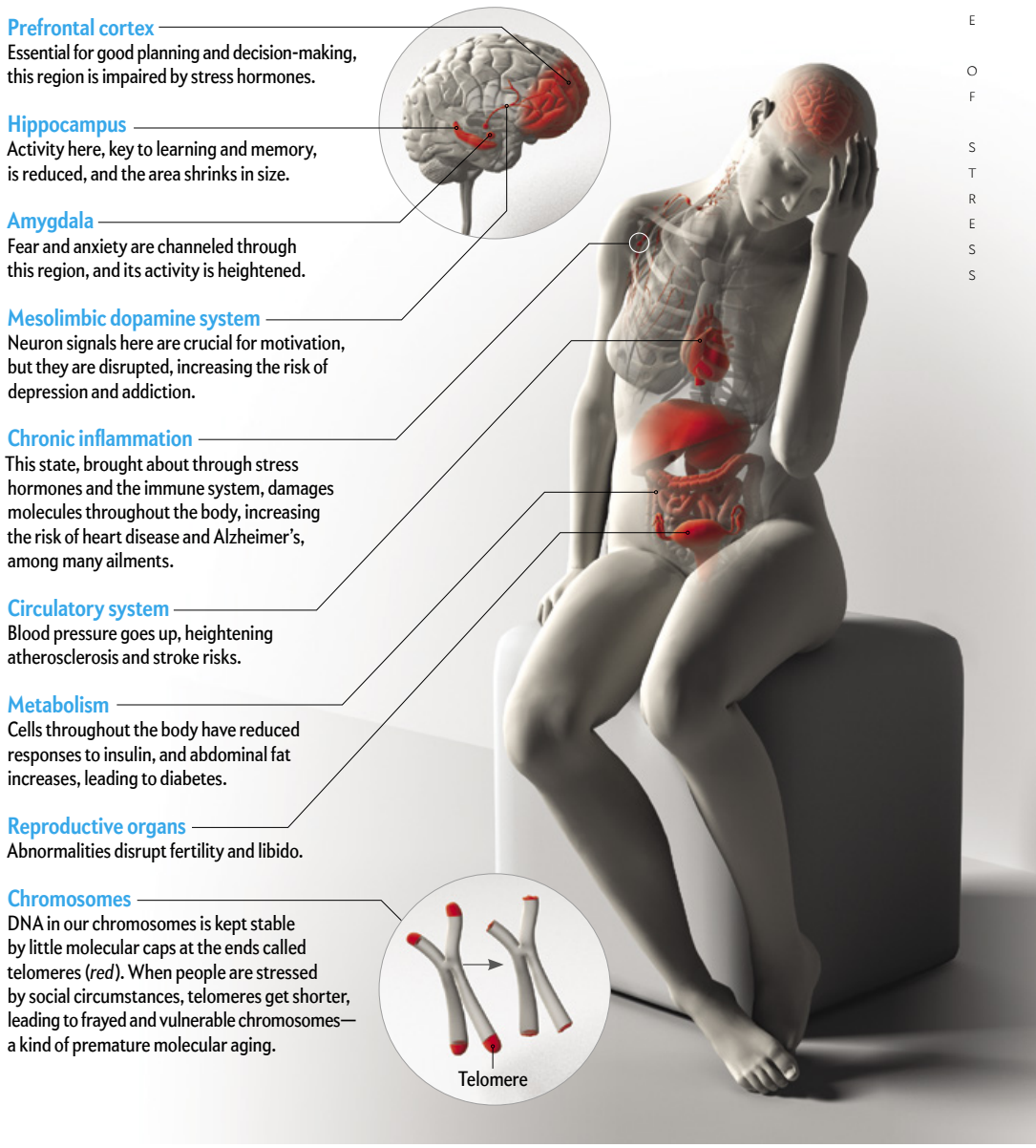
Prefrontal cortex
Essential for good planning and decision-making, this region is impaired by stress hormones.
Hippocampus
Activity here, key to learning and memory, is reduced, and the area shrinks in size.
Amygdala
Fear and anxiety are channeled through this region, and its activity is heightened.
Mesolimbic dopamine system
Neuron signals here are crucial for motivation, but they are disrupted, increasing the risk of depression and addiction.
Chronic inflammation
This state, brought about through stress hormones and the immune system, damages molecules throughout the body, increasing the risk of heart disease and Alzheimer's, among many ailments.
Circulatory system
Blood pressure goes up, heightening atherosclerosis and stroke risks.
Metabolism
Cells throughout the body have reduced responses to insulin, and abdominal fat increases, leading to diabetes.
Reproductive organs
Abnormalities disrupt fertility and libido.
Chromosomes
DNA in our chromosomes is kept stable by little molecular caps at the ends called telomeres (*red*). When people are stressed by social circumstances, telomeres get shorter, leading to frayed and vulnerable chromosomes—a kind of premature molecular aging.
Telomere

Illustration by Bryan Christie Design

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THE HEALTH OF NATIONS AND STATES

Around the world, health and social problems grow as income disparities widen within societies. Epidemiologists Richard Wilkinson and Kate Pickett demonstrated this connection in their 2009 book *The Spirit Level.* They ranked countries by an economic measure from the United Nations called the 20:20 ratio, which compares how much richer the top 20 percent of people are than the bottom 20 percent.

As the gap widened, a combined index of life expectancy, infant mortality, mental health issues, obesity and other problems got worse. Average income in these countries does not explain this trend. In U.S. states, researchers found a similar effect. They ranked states using a U.S. Census Bureau measure called the Gini coefficient, which compares incomes among all population members, not just select groups. Again, the trend of bad health effects strongly followed inequality and could not be explained by average income in a state.

Health and social problems are worse in countries with more income inequality
Index of Health and Social Problems
Worse
Better
Overall trend
Low
High
Income Inequality, 2005 (20:20 ratio)
Higher average income levels in countries do not mean better health
GDP per Capita, 2005 (U.S. dollars, at purchasing power parity)
U.S. states also show worse health and social problems as income inequality climbs
Income Inequality, 1999 (Gini coefficient)
U.S. states with higher average incomes rarely show improved health
Per Capita Income, 1999 (dollars)

Index of Health and Social Problems includes these components:

- Life expectancy
- Teenage births
- Obesity
- Mental health
- Homicides
- Imprisonment
- Trust/mistrust
- Education
- Infant mortality rate
- Social mobility (for country level only)

were, even after the researchers accounted for potentially confounding factors such as diet and smoking. Telomeres normally shorten at a more or less constant rate in people, and calculations showed that these women's telomeres had aged roughly an additional decade—and sometimes more—past those in the low-stress group.

This discovery triggered a flood of supporting studies showing that stressors that included major depression, post-traumatic stress disorder and the experience of racial discrimination can all accelerate telomere shortening. Unsurprisingly, lower childhood SES also predicts shorter telomeres in adulthood; perceived poor neighborhood quality, witnessing or experiencing violence, family instability (such as divorce, death or incarceration of a parent), and other features of poor status early on are tied to these shrunken chromosome tips later in life. Spend your childhood in poverty, and by middle age your telomeres will probably be about a decade older than those of people with more fortunate childhoods.

Thus, from the macro level of entire body systems to the micro level of individual chromosomes, poverty finds a way to produce wear and tear. Most studies of telomere length compare "poor" with "non-poor," as do the studies comparing allostatic load, but the few studies that examine the whole spectrum of inequality, step by low-status step, show that every rung down the SES ladder most likely worsens these biological markers of aging.

OUT OF CONTROL

SLIPPING DOWN these rungs also changes the brain and behavior, according to a slew of recent neurobiological studies. My laboratory has devoted a quarter of a century to studying what ongoing stress does to the brain in rodents, monkeys and humans. Along with other labs, we have learned that one hotspot is the hippocampus, a region critical to learning and memory. Sustained stress or exposure to excessive glucocorticoids impairs memory by lowering hippocampal excitability, retracting connections between neurons and suppressing the birth of new neurons. In the amygdala, a different brain area that is central to fear and anxiety, stress and glucocorticoids heighten those two reactions. Instead of damping things down as they do in the hippocampus, in this fear-promoting region they increase excitability and expand neuronal connections. Together these findings help to explain

THE SPIRIT LEVEL: WHY GREATER EQUALITY MAKES SOCIETIES STRONGER, BY KATE PICKETT AND RICHARD WILKINSON. BLOOMSBURY, 2009; BUREAU OF ECONOMIC ANALYSIS, U.S. DEPARTMENT OF COMMERCE (*U.S. income per capita data*); *HUMAN DEVELOPMENT REPORT 2007/2008: FIGHTING CLIMATE CHANGE: HUMAN SOLIDARITY IN A DIVIDED WORLD.* UNITED NATIONS DEVELOPMENT PROGRAM, 2007 (*GDP per capita data*)

Graphics by Jen Christiansen

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why post-traumatic stress disorder atrophies the hippocampus and enlarges the amygdala. Another affected area is the mesolimbic dopamine system, which is crucial to reward, anticipation and motivation. Chronic stress disrupts that system, and the result is a predisposition toward the anhedonia of depression and vulnerability to addiction.

Bombardment by glucocorticoids also affects the prefrontal cortex (PFC), key to long-term planning, executive function and impulse control. In the PFC, social stress and elevated glucocorticoids weaken connections between neurons, making it harder for them to communicate. Myelination, the process that insulates cables between neurons and thus helps them pass signals faster, is impaired. Total cell volume in the region declines, and chronic inflammation is activated.

What happens when the PFC is impaired in this way? Lousy, impulsive decisions happen. Consider "temporal discounting": when choosing between an immediate reward and a bigger one if you wait, the appeal of waiting goes down as the time you have to wait goes up. The PFC is normally good at combating this shortsightedness. But stress steepens temporal discounting; the more cumulative stress, the less PFC activation in experiments that call for gratification postponement. For people sliding further into inequality, the less active PFC makes it harder for the brain to choose long-term health over immediate pleasure. That neurological effect can explain why people with more total life stress gain more weight and smoke and drink more than people with fewer stressors.

These changes in the PFC happen in children, too. In separate studies, Martha Farah of the University of Pennsylvania and W. Thomas Boyce, professor emeritus at U.C.S.F., observed that lower-SES kindergartners typically have elevated glucocorticoid levels, a thinner and less active PFC, and poor PFC-dependent impulse control and executive function. These effects increase as kids get older. By adolescence, lower SES predicts smaller PFC volume. By adulthood, low SES predicts steeper temporally discounted decisions.

Some of these observations present a tricky chicken-and-egg question. The brain changes could lead to poor choices, which in turn lead to deeper poverty, rather than the other way around. But the research suggests that causes and effects run in the other direction, with SES and inequality first influencing PFC function and then other bad things happening.

For example, kindergartners' SES predicted their PFC function; few five-year-olds plummet into poverty by squandering their paychecks on drink and horses. Further evidence comes from a 2013 study by Jiaying Zhao of the University of British Columbia and his colleagues. They examined Indian farmers whose economic fortunes vary seasonably. As individuals' SES went from being poorest during planting season to wealthiest after harvest, improvements in PFC function followed.

To me, the most important evidence comes from research in which people's sense of their SES was lowered by the design of the experiment. Afterward these individuals did heavier temporal discounting. In one 2012 study, subjects played a game of chance against one another, with differing amounts of starting resources. "Poor" subjects became more likely to borrow against future earnings and less attuned to helpful clues about game strategy.

In another study, subjects who were prompted to imagine scenarios of financial loss (versus neutral or advantageous ones) did steeper temporal discounting in an unrelated task. In still other research, subjects were primed to imagine their financial burdens by contemplating an expensive car repair; cognitive function was unchanged in high-SES subjects but declined in poorer individuals.

Why should a transient sense of lower SES induce cognitive changes typical of lower SES in the real world? One explanation is that it is a rational response because it is hard to think about squirreling away money for old age if you can barely buy groceries. Poverty makes the future a less relevant place.

But there is also a powerful stress-related explanation: long-term planning and impulse control tires out the PFC. Increase subjects' cognitive "load" with taxing PFC-dependent tasks, and they become more likely to cheat on their diet. Or you can—and scientists have done this—increase cognitive load by tempting dieting subjects with snacks, and then they do worse on PFC-dependent tests. How much this represents literal "depletion" of the PFC metabolically versus declining motivation is unclear.

Either way, lower SES creates chronic financial worry that distracts and exhausts. It is hard to ace a psychological task of, say, subtracting a series of numbers or a more important task of reining in your drinking when you are worrying about paying your rent. One finding in the car-repair study supports this interpretation. When subjects contemplated a repair of negligible cost, low- and high-SES subjects performed equally well on cognitive tasks.

Of course, we need to better understand the biological consequences of inequality and learn better ways to heal its health scars. But frankly, right now we know quite a bit. We know enough to prompt moral outrage at the situation. It is outrageous that if children are born into a disadvantaged family, they will be predisposed toward poor health by the time they start to learn the alphabet. It should not require us to measure inflammation or the length of chromosomes to prove this is wrong, but if it does, more power to this science. SA

Robert M. Sapolsky is a professor of biological sciences, neurology and neurological sciences at Stanford University and a research associate at the National Museums of Kenya. In his laboratory work, he focuses on how stress can damage the brain and on gene therapy for the nervous system. He also studies populations of wild baboons in East Africa, trying to determine the relation between the social rank of a baboon and its health.

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TREATING A TOXIN TO LEARNING

Stress may be silently sabotaging success in school. Its effects are especially potent for children in poverty

By Clancy Blair

STRESS CAN BE TOXIC AT ANY AGE. IT RATTLES US WHEN IT STRIKES, shaking up our relationships and narrowing our focus. When it becomes chronic, it ravages our health. Physically, emotionally and intellectually, stress can drag us down.

An even more insidious effect is the assault it can launch on a child's brain, impeding the development of critical cognitive skills. A number of researchers, including myself, have discovered that psychological stress affects the thinking skills and brain development of even very young children, likely beginning prenatally. It is no mystery that stress thrives in difficult situations, but research is now showing that a disadvantaged upbringing may set back children in profound ways. In fact, stress may be one important mechanism through which poverty adversely affects children's ability to perform well in school.

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Although children differ in their susceptibility to the problems of poverty, data show that youngsters from lower-income households are very likely to start school behind their more affluent peers. This socioeconomic gap persists throughout the school years and is difficult to close. People have long argued that disadvantaged homes tend to offer an impoverished learning environment that does not sufficiently prepare children for the rigors of school. This well-established fact is, at best, only half of the story. My work suggests that, in addition to the absence of beneficial things such as rich language stimulation and plentiful learning materials, poverty is also characterized by the presence of detrimental things, such as crowded conditions, noise, financial worries and an inability to provide adequate child care—all of which directly impairs specific learning abilities in children.

A stressful childhood may emerge from conditions other than poverty, whether from challenging family circumstances such as a divorce or death, overbearing or distracted parents, or any factors at home or at school that create anxiety. A focus on reducing stress through changes in the home or in the classroom could improve the well-being of large numbers of schoolchildren and set them up for greater success throughout life.

A LITTLE STRESS HEIGHTENS ALERTNESS; IT IMPROVES PEOPLE'S PERFORMANCE ON COMPLEX TASKS. BUT AS THE DOSE EXCEEDS A CERTAIN LEVEL, STRESS STARTS TO ERODE PERFORMANCE.

FLOODING THE ENGINES

STRESS HORMONES can shape the developing circuitry of the brain. Most notably, they influence the neural connections in the prefrontal cortex, located behind the forehead, that buttress what are known as executive functions. These include the ability to hold information in mind (working memory), to inhibit automatic or impulsive responses to stimulation, and to flexibly shift attention. Executive functions are critical for reasoning, planning and problem-solving and for regulating emotions and attention. They are essential to academic success.

The effects of stress on the brain depend on how much of it is present. A little stress heightens alertness; it improves people's performance on complex tasks. But as the dose exceeds a certain level, stress starts to erode performance. This relation between arousal and performance can be expressed as an inverted U-shaped curve, first identified by psychologists Robert Yerkes and John Dodson in 1908. In the brain, moderate amounts of stress hormones such as cortisol and noradrenaline boost activity in prefrontal areas that underlie executive functions. At high levels, however, they flood this engine of self-regulation, shutting it down. Over time the brain circuits that control stress hormone levels are shaped by experience toward a tendency to unleash either very large or very small amounts of these hormones onto the prefrontal cortex in response to stress or to maintain a more optimal level of arousal.

In 2001 I began to wonder how this physiology played out in the brains of young children and whether it might explain how poverty "gets under the skin." I set out to explore whether the chronic stress of poverty might be impairing the developing executive function of children enough to set them back at school.

My graduate student at the time, Rachel Peters, and I, then at Pennsylvania State University, gave two tests to 170 four-year-olds in central Pennsylvania enrolled in Head Start, the federal preschool program for children in poverty. We measured mental flexibility by asking children to identify different ways in which small groups of objects were similar. We examined working memory and inhibitory control by asking them to tap a peg twice when the experimenter tapped it once, and vice versa. Here the child had to remember the rule and control the impulse to copy the experimenter. We also asked teachers to rate each child's behavior and academic abilities. And in collaboration with neuroendocrinologist Douglas Granger, also then at Penn State, we took samples of the children's saliva to determine levels of cortisol at the beginning, middle and end of our experimental session.

The children with better executive function and behavior had low cortisol at the beginning of the session that rose and then returned to baseline, as expected, in response to the mild stress of meeting one of us and participating in our tasks. Those who showed either a sustained high level of cortisol or a blunted response—high initial levels that then dropped, indicating a shutting down of the process—tended to have low executive function; their teachers also rated them as more aggressive and lacking in self-control. We published these results in 2005.

As we followed these children into kindergarten, we observed that executive function matters for achievement: this suite of mental skills was the main determinant of math proficiency, far outweighing other aspects of intelligence. And an analysis published in 2012 by our team, led by Daniel Berry, now at the University of Minnesota, found that elevated cortisol in children predicts academic difficulties, as indicated by knowledge of math, letters and words. Our analysis suggested that this effect occurs through detriments to executive function—as opposed to, say, low general mental ability—demonstrating that these thinking skills are the critical link tying high cortisol to low academic ability.

POSITIVE PARENTING

MEANWHILE my colleagues and I also set out to determine what aspects of poverty might contribute most to children's stress. We focused on parenting style. Because of the stressful circumstances in which they find themselves, parents in poverty tend to elicit obedience through discipline rather than encouraging exploration and learning by doing. The latter approach, known as scaffolding, is essential to sensitive parenting. In this type of parenting, mothers and fathers interact with their children during play and create opportunities for them to accomplish small tasks, such as stacking blocks. Although impoverished parents can and do provide sensitive care, they are less likely to do so, given the realities of their situation and, potentially, their own high stress levels.

To investigate further, we have been following 1,292 children, starting at birth, and their families, most of whom live in poverty in rural communities in Appalachia and

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the Deep South. For more than 17 years now our team has been visiting these homes annually to collect data on family and economic conditions, as well as on executive function and cortisol levels. My colleagues Martha Cox of the University of North Carolina at Chapel Hill and Roger Mills-Koonce, now at U.N.C. Greensboro, analyzed video recordings of mothers interacting with their children in free play. In our first analysis, published in 2008, we found that infants whose mothers displayed the sensitive, scaffolding parenting style had lower cortisol levels and were calmer and more attentive than those whose mothers either completed the activity for them or restricted their attempts to do so.

Furthermore, at age seven months the children whose parents displayed the positive parenting style were more likely to show a healthy cortisol response—a rise and fall—to fear (triggered by an experimenter in a mask) and frustration from a toy placed just out of reach. At age 15 months these children again had lower cortisol levels and were more likely to respond appropriately to the emotional challenges. We now had evidence that parenting style shapes the developing stress-response system.

We next sought to sketch the complete path from poverty to parenting to increased stress and diminished executive function in the same group of children. We found that the more severely impoverished the family, the less likely parents were to be sensitive and responsive. As expected, the children in such homes had elevated cortisol, which was, in turn, associated with lower executive function. We also saw that less positive parenting went hand in hand with poorer executive function in children, indicating that mothers and fathers can directly stimulate the development of important mental skills.

CREATING CAPABLE KIDS

RESEARCH INDICATES that stress from a variety of sources—chaotic and poorly run classrooms, for example, or problems with family or peers—impedes learning. The potential good news: knowing that stress is a malevolent force means that finding ways to thwart it could boost children's learning capacity.

In that vein, my collaborators and I have tested a program that teaches parents how to be more sensitive and how to structure opportunities for their children to learn while providing warm and loving care. We have also shown that an innovative curriculum that gives kindergarteners and preschoolers more control over their learning activities has large effects on learning and executive functions for children in high-poverty schools. Although this work is in its early stages, we are encouraged by the possibility that informed changes to environments can boost children's self-control and academic competence, giving many of our youth a far greater chance of succeeding in life. SA

CHILDREN WHOSE PARENTS encourage them to learn by doing are calmer and more attentive than those whose mothers and fathers typically restrict them or do things for them.

Clancy Blair is professor of applied psychology at New York University, where he studies the development of self-regulation in early childhood. He earned his Ph.D. in 1996 from the University of Alabama at Birmingham. His research is supported by the National Institutes of Health.

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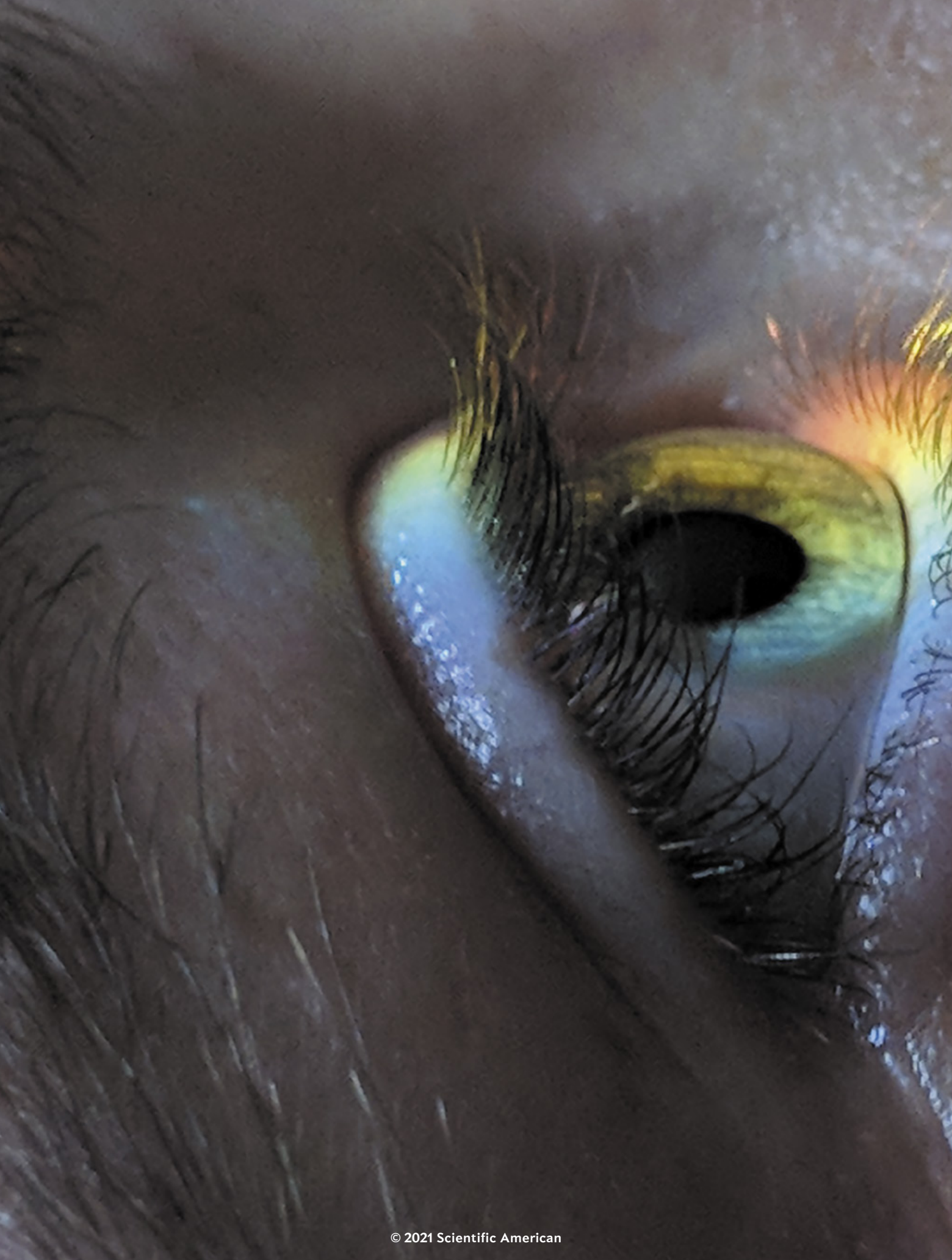

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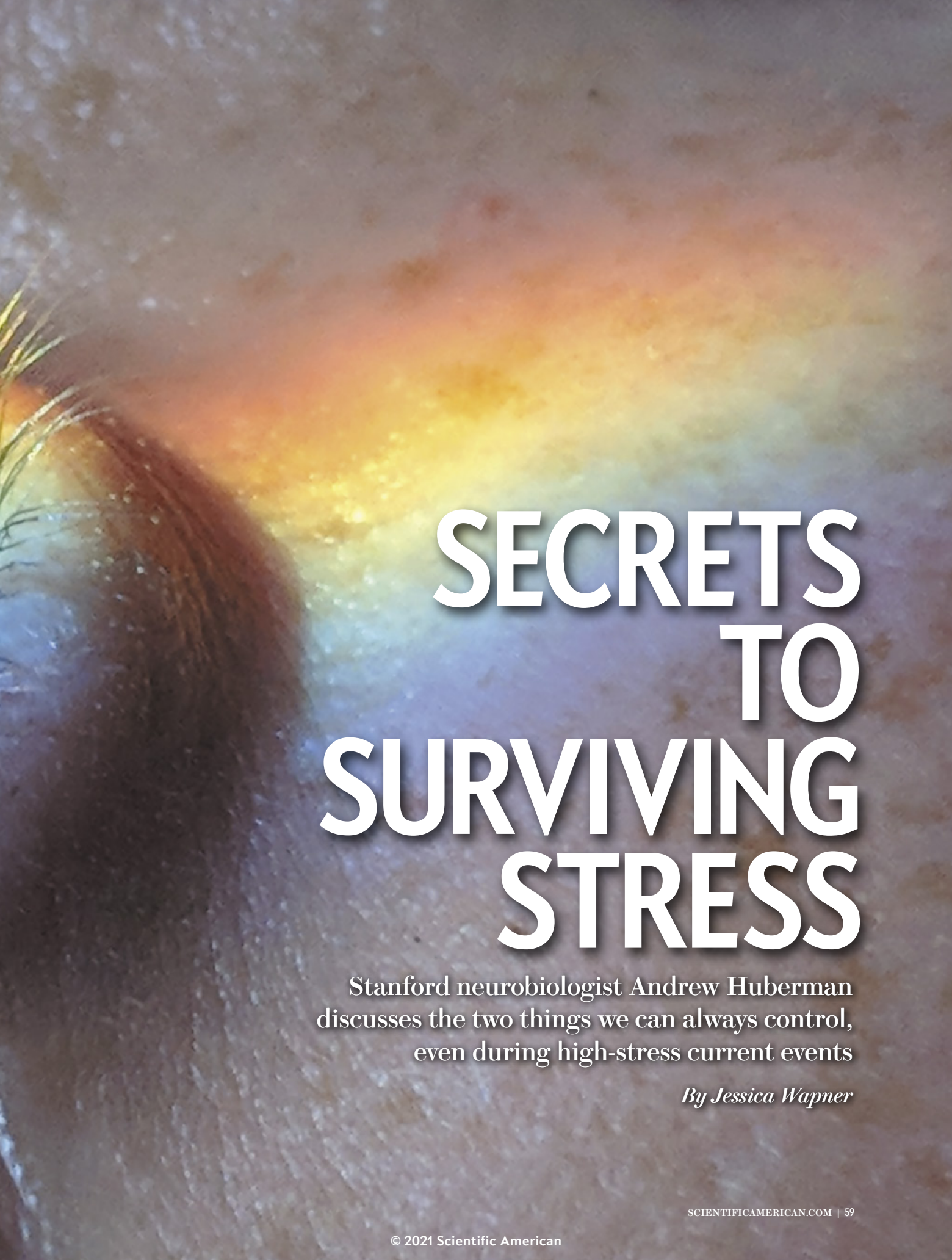

SECRETS TO SURVIVING STRESS

Stanford neurobiologist Andrew Huberman discusses the two things we can always control, even during high-stress current events

By Jessica Wapner

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WE ARE LIVING THROUGH AN INARGUABLY CHALLENGING TIME. Earlier this year the U.S. faced its highest daily COVID-19 case counts yet. Uncertainty and division continue to dog the aftermath of the presidential election. We are a nation and a world under stress.

But Andrew Huberman, a neuroscientist at Stanford University who studies the visual system, sees matters a bit differently. Stress, he says, is not just about the content of what we are reading or the images we are seeing. It is about how our eyes and breathing change in response to the world, as well as the cascades of events that follow. Both these bodily processes also offer us easy and accessible releases from stress.

Huberman's assertions are based on both established and emerging science. He has spent the past 20 years unraveling the inner workings of the visual system. In 2018, for example, his laboratory reported its discovery of brain pathways connected with fear and paralysis that respond specifically to visual threats. And a small but growing body of research makes the case that altering our breathing can alter our brain. In 2017 Mark Krasnow of Stanford, Jack Feldman of the University of California, Los Angeles, and their colleagues identified a tight link between neurons responsible for controlling breathing and the region of the brain responsible for arousal and panic.

This growing understanding of how vision and breathing directly affect the brain—rather than the more nebulous categories of the mind and feelings—can come in handy as we continue to face mounting challenges around the globe, across the U.S. and in our own lives. SCIENTIFIC AMERICAN spoke with Huberman about how it all works.

[*An edited transcript of the interview follows.*]

What is stress?

Stress is one position along the continuum of what we call autonomic arousal. At one end of this continuum would be somebody in a coma. At the very other end of that continuum is a full-blown panic attack: heart racing, pupils dilating, hyperventilating. In between we have lower levels of stress [and the states of being] alert and focused, sleepy and asleep. Stress is generally a high level of autonomic arousal. It was designed to be a generic response to mobilize the body.

Sometimes that's well matched to the demands of life. If you need to run and catch your train, you want all the things that go along with stress to go pursue that train. But if the stress response is spontaneous or excessive, it can start to feel pathological.

What is stress's relationship to vision?

When you see something exciting or stressful—a news headline, a fraudulent credit-card charge—heart rate increases; breathing increases. One of the most powerful changes is with vision. The pupils dilate, and there's a change in the position of the lens in the eye. Your visual system goes into the equivalent of portrait mode on a smartphone. Your field of vision narrows. You see one thing in sharper relief, and everything else becomes blurry. Your eyeballs rotate just slightly toward your nose, which sets your depth of field and focus on a single location. This is a primi-

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tive and ancient mechanism by which stress controls the visual field.

How does this visual mode affect the body?
This focal vision activates the sympathetic nervous system. All the neurons from your neck to the top of your pelvis get activated at once and deploy a bunch of transmitters and chemicals that make you feel agitated and want to move.

Why is the visual field so connected to this brain state?
Something that most people don't appreciate is that the eyes are actually two pieces of brain. They are not connected to the brain; they are brain. During development, the eyes are part of the embryonic forebrain. Your eyes get extruded from the skull during the first trimester, and then they reconnect to the rest of the brain. So they're part of the central nervous system.

Having the eyes outside the skull orients the organism to the time of day. But it also means that you've got two pieces of brain that can register events in the environment at a distance in order to adjust the overall state of alertness in the rest of the brain and body. It would be terrible if we had to wait until things were in contact with us before we could prepare to react to them.

Is there a visual mode associated with calmness that can change our stress levels?
Yes: panoramic vision, or optic flow. When [you] look at a horizon or at a broad vista, you don't look at one thing for very long. If you keep your head still, you can dilate your gaze so you can see far into the periphery—above, below and to the sides of you. That mode of vision releases a mechanism in the brain stem involved in vigilance and arousal.

We can actually turn off the stress response by changing the way that we are viewing our environment, regardless of what's in that environment.

You are also researching breathing as a way to regulate autonomic arousal.
Yes. Vision and breathing are, without question, the fastest and most obvious ways to control autonomic arousal. The way we breathe impacts our states of stress very strongly.

Data show that during sleep and claustrophobic states, people and animals generate what are called physiological sighs—double inhalations followed by exhalations. Children also do this when they are sobbing. A physiological sigh, two or three times, is the fastest way that we are aware of to bring the level of autonomic arousal back down to baseline.

Why does this breathing pattern work to reduce stress?
Our lungs consist of tons of tiny little sacs of air—millions of sacs of air. As we get stressed, these little sacs collapse. They deflate like a balloon. Physiological sighs cause the sacs to reinflate. Carbon dioxide is the trigger for breathing: We don't breathe because we need oxygen. We breathe because carbon dioxide levels get too high. Physiological sighs offload the maximum amount of carbon dioxide.

How are you studying the link between breathing and stress?
David Spiegel, associate chair of psychiatry at Stanford, and I are leading a study of breathing in which 125 participants have been wearing wrist monitors that measure breathing, sleep duration, heart rate variability and heart rate. The participants are divided into four groups of different breathing modalities: meditation for five minutes a day; repeated physiological sighs; box breathing (equal durations of "inhale, hold, exhale, hold," repeated for five minutes); and deliberate hyperventilation repeated a few times. We want to see which patterns of breathing most rapidly reduce the stress response. We're analyzing the data now.

How are breathing and the brain connected?
The relationship is anchored through the diaphragm, the only organ in the body that is skeletal muscle designed for voluntary movement. You can immediately take control of the diaphragm. So breathing represents a bridge between the conscious and unconscious control of the body.

When you inhale, the diaphragm moves down, and the heart gets a little bigger because it has more space. Blood flows a little more slowly through the heart under that condition. So the heart then signals to the brain, and the brain says, "Oh, we'd better speed up the heart." So if you want to increase your heart rate, you inhale more than you exhale. The opposite is also true. Every time you exhale, you're slowing down the heart rate.

So with vision and breathing, you are looking at physiological processes that are automatic but that we can also control.
Yes. If I make you stressed, you'll perspire. But you wouldn't say, "I'm going to make myself sweat, and therefore I'll be stressed." You can't control your heart rate directly. You can't control your adrenals with your mind. But you can control your diaphragm, which means you control your breathing, which means you control your heart rate, which means you control your alertness. You can control your vision, which thereby controls your level of alertness, your level of stress and your level of calmness.

Vision and breathing are essential as levers or entry points to autonomic arousal because they are available for conscious control at any point. SA

Jessica Wapner is a science writer and author of *The Philadelphia Chromosome: A Genetic Mystery, a Lethal Cancer, and the Improbable Invention of a Lifesaving Treatment* (The Experiment, 2014).

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STOP DOOMSCROLLING NEWS AND SOCIAL MEDIA

"Doomscroll Reminder Lady" Karen K. Ho explains how to step away from the screen

By Sophie Bushwick

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READING THROUGH THEIR SOCIAL MEDIA FEEDS, AMERICANS ARE LIKELY to encounter anguished accounts of political turmoil, the coronavirus pandemic and continued fallout from cyberattacks, among other less than cheerful topics. And yet many can't stop scrolling even more, perhaps hoping to distract themselves from thinking too hard about any one of these ongoing problems. The practice has earned a suitably apocalyptic nickname: doomscrolling.

In spring 2020, at the start of the global pandemic, Karen K. Ho, a global finance and economics reporter at the news site Quartz, began tweeting regular reminders to step away from the screen and do something that will actually make a doomscroller feel better—such as getting a drink of water, stretching or simply going to bed on time. "Those first couple of months I was basically talking out loud to myself," she says. But her alerts drew attention from mainstream news outlets as well as fellow social media users, and in the year that followed, Ho's Twitter following doubled to more than 44,000. "It was helping people feel less alone about a practice that they knew to be harmful, and me trying to offer a solution in a way that isn't antagonistic or judgmental," she explains. "I think the thing that was really surprising to people was how consistent I was because right now nothing's really consistent. It's all really chaotic. And they felt like somebody was looking out for them."

SCIENTIFIC AMERICAN asked Ho what her project has taught her about why people doomscroll—and how they can stop. "What doomscrolling does is rob future you of the energy you need to really focus on important things," she says, "and also to take better care of yourself."

[*An edited and condensed transcript of the interview follows.*]

Doomscrolling makes us feel bad—so why do we do it?

It's a combination of a couple of things. There is the very nature of the design of these applications. It's the slot machine effect: The old way was, you would find something really funny, educational or informative, and the surprise was not knowing when that moment of dopamine or delight would hit you. Then there's the compulsion for many people to be better informed about the chaotic situation that many of us are currently in as a result of the pandemic, the uncertainty regarding the economic recession, as well as the social justice situation affecting many minorities, women and vulnerable groups in the United States and around the world. Then I think, finally, it's a very limited act of agency that people still have. You and I can't go to our favorite restaurants, entertainment

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venues, gyms; we can't interact with friends and loved ones because of physical distancing measures. People can't do a lot of other normal behaviors, so they're able to exercise their agency in this limited way, even if it's detrimental to their ability to get a good night's sleep or reduce their stress.

What can we do to prevent ourselves from endlessly scrolling?

I am a firm believer in using technology. New phones have ways for you to better focus: You can set manual time limits and hours in which you can't open the apps themselves. I've also used apps like the Chrome extension "Stay Focused" a couple of times, where you can set various time limits for checking [social media] on your computer. I also just manually log out on my work computer and my cell phone; I try to increase the friction required to log in and read the Web site. Then there's the emergency function: you literally just change the account password and give it to someone else so you can't log in.

I use a lot of operations management and scientific methods to get myself to not look at my phone. If you're going to pick up your phone more [at night], you have to put a book where your phone would normally be when you're not at work, to read that before you go to bed. One of the best tips is, I watch a lot of TV and movies with subtitles—like in foreign languages. Because you can't look at your phone, you have to read what's on the screen to understand what's going on. When it's warmer, do things outside where you can't look at your phone. (When spring comes, I'm going to bike so much!) Also, I find other tactile hobbies, like puzzles or Lego, to be really helpful. A lot of people have turned to writing cards and letters as an alternative activity during the pandemic. Some people like cooking, some people bake—it's really about personal psychology. Like, if you're fidgeting, it's just you feeling anxious about something. That's why you're checking Twitter, so that you're not thinking about the anxiety. Can you call a friend or a family member whom you haven't spoken to in a while instead of looking at your phone?

It's also about reminding myself constantly of things that sound really hokey and mindful. What I really remind myself of, repeatedly, is that when I die, Twitter means nothing. No one will be like, "I went viral a lot." They'll be like, "Did I have enough energy to do my job pretty well? Do the people we love know that we love them?" I think those are the things to really invest energy in.

Is there any way to snap yourself out of a scrolling session once you start?

Prevention is always better than [trying to stop] while you are in the middle of it. But if you're in the middle of it—that's why I send the reminders. I'm trying to meet people where they already are. There are several other Twitter accounts, like @tinycarebot, that are designed to catch you in the middle of doing it. And then there are alarms. I set alarms on my phone to be loud and obnoxious and say, "Hey, it's late. You should probably be going to bed." It's just setting yourself up, even before you start—ask "What are the processes to improve your rates of success?" Even if you go down the wrong path, how can you course-correct?

What are some other things to know about doomscrolling?

The thing to remember is that there are limits to individual responsibility and reminders to take care. Fundamentally it is an irrational response to a reasonable emotion—like about how frustrating it is to see the vaccine rollout be screwed up or the lack of mask mandates. There are lots of medical people who follow me because of the reminders, a lot of science reporters and health reporters, and they're doomscrolling because of repeated systemic failures by people in power. Doomscrolling existed for the Black community long before everybody else discovered it in 2020: when Black Americans are killed or hurt by police officers, there's a hashtag for their name.

A lot of doomscrolling is that feeling of lack of direction and helplessness. Doing something, having a series of steps for people to do, I find reduces their stress. So that's why you see me recommend drinking water or stretching—because unconsciously people let these things slide. When in doubt, I also find donating money makes you feel less helpless. It's not fair that people should [only] think about all of these huge, big-picture problems; this small thing you can do is go to sleep right now, instead of staying up late. SA

YOU AND I CAN'T GO TO OUR FAVORITE RESTAURANTS, ENTERTAINMENT VENUES, GYMS; WE CAN'T INTERACT WITH FRIENDS AND LOVED ONES BECAUSE OF PHYSICAL DISTANCING MEASURES. PEOPLE CAN'T DO A LOT OF OTHER NORMAL BEHAVIORS, SO THEY'RE ABLE TO EXERCISE THEIR AGENCY IN THIS LIMITED WAY, EVEN IF IT'S DETRIMENTAL TO THEIR ABILITY TO GET A GOOD NIGHT'S SLEEP OR REDUCE THEIR STRESS.

Sophie Bushwick is an associate editor at *Scientific American*, covering technology.

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HEAD STRONG

For many people with depression, exercise may be the most effective, least expensive and safest treatment

By Ferris Jabr

Photograph by Aaron Goodman

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ON VALENTINE'S DAY 2014 JACK METTA (THEN KNOWN AS ELIZABETH Droge-Young) admitted themself to a hospital in Syracuse, N.Y. For more than a year they had been struggling with depression—not eating well and losing interest in the movies, books and music that usually delighted them. They had withdrawn from friends and were routinely missing classes at Syracuse University, where they were a fifth-year graduate student in evolutionary biology. Some days that winter they could not even make it out of bed, despite the fact that they had started taking antidepressants the previous fall. In their darkest moments, obsessive and frightening thoughts of self-harm and suicide flooded their mind. "It was horrible," Metta recalls. "I felt very unsafe." They realized they needed a serious intervention.

After a week and a half on suicide watch at the hospital, plus a stronger cocktail of medications, Metta returned home, taking an academic leave of absence for the remainder of the school year. For a while they seemed to be getting better. But when they went back to school in August 2014, the unbearable sadness and dark impulses resurfaced. This time Metta turned to a hospital in Saratoga Springs, N.Y., some two and a half hours away, that offered a more holistic treatment. In addition to medication and counseling, their doctors prescribed a full schedule of daily activities such as arts and crafts and walks around the grounds. During their stay, a hospital therapist also recommended exercise. So after leaving the hospital, Metta started going to the gym three to five times a week, walking and jogging on the treadmill, lifting weights and attending Zumba, a popular dance fitness class.

"It was empowering," says Metta, now 37 and living in Denver. "It really helped with my mood. There's something wonderful about the mind-body connection exercise provides. Using weight machines or jogging on the treadmill allows you to be self-reflective: 'Look at the strength and endurance I have. This is something positive about myself.' And the dancing was joyful—just being able to move around in a way that was free and felt good." Since incorporating exercise into their regimen for managing depression, Metta has never relapsed to the point of requiring another hospitalization. To this day, they continue to incorporate movement into their daily routine as much as possible.

The fact that exercise improves physical health is so well known as to be a platitude. Decades of research demonstrate that regular exercise lowers the risk of many illnesses—heart disease, diabetes, cancer—and extends the average life span. In contrast, the benefits of exercise for mental health are not quite so obvious or well publicized. We work out to "get in shape," and some of us depend on bike rides, neighborhood jogs or yoga to help clear our mind and relieve stress. But how often do we seriously consider exercise as a viable treatment for mental illness, one just as effective as medication or counseling? Can a steady routine of physical workouts really help to keep psychological disorders in check?

In the case of depression, the collective evidence to date suggests that the answer is an emphatic yes. Exercise is by no means a panacea, and in severe cases of depression, it may be futile on its own. But scores of experiments now show that exercise is much more than a temporary distraction from mental woes or some ultimately inconsequential palliative. It appears to combat depression in a number of ways: by strengthening our biochemical resilience to stress, encouraging the growth of new brain cells, bolstering self-esteem and possibly even counterbalancing an underlying genetic risk for mental illness. For most people with mild to moderate depression, exercise is one of the strongest, safest, most practical, most affordable and even most enjoyable treatments available.

"I am a big believer in the value of physical activity," says clinical psychologist James Blumenthal of Duke University. "The majority of evidence suggests that a certain subset of patients can benefit just as much with exercise, if not more, as with medication." Psychiatrist Madhukar Trivedi of the University of Texas Southwestern Medical Center, who has studied the relation between exercise and mental health for almost 20 years, agrees: "We have now generated a whole big body of literature about

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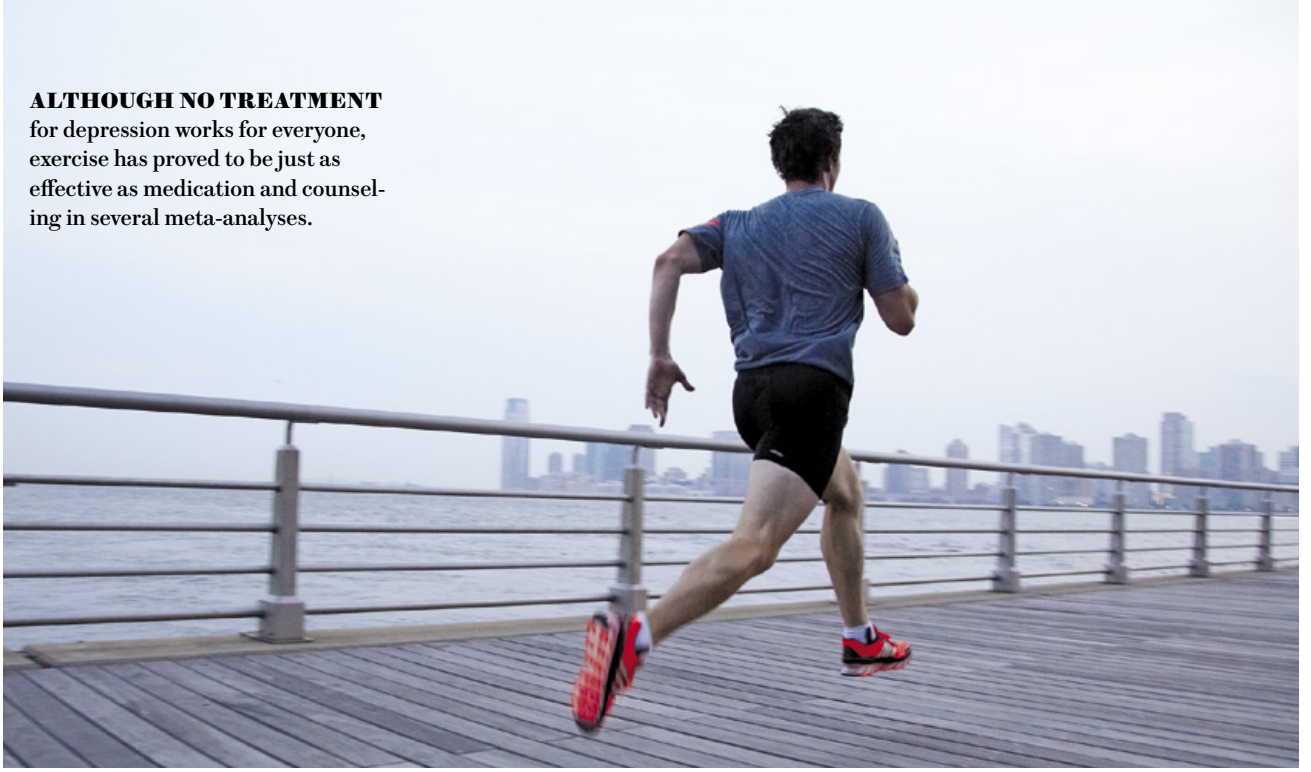

ALTHOUGH NO TREATMENT for depression works for everyone, exercise has proved to be just as effective as medication and counseling in several meta-analyses.

CHRIS TOBIN *Getty Images*

exercise as a treatment for depression. We've looked at dose, at adding exercise as an augmentation treatment, at specific biomarkers associated with improvement. We have the studies to show that something really powerful and interesting is going on."

ON THE STRENGTH OF THE EVIDENCE

MAJOR DEPRESSION—an illness characterized by a persistent low mood or loss of interest in typically pleasurable activities, often accompanied by insomnia, fatigue, poor concentration or feelings of worthlessness—is one of the leading causes of disability and death around the globe, according to the World Health Organization. At any given time, it afflicts around 350 million people worldwide and 18 million people in the U.S. Only a fraction of sufferers seek help, and of those, only a third respond to standard treatment, which is usually counseling and medication. Antidepressant drugs are often costly and can have serious side effects, driving many patients to search for less expensive, safer, more natural solutions. In a survey of more than 2,000 U.S. adults published in 2001, more than half of the respondents with depression said that they had turned to some kind of alternative treatment, such as yoga, herbal medicines or acupuncture.

Psychologists and clinicians have studied exercise as an alternative treatment for depression for at least 30 years. Blumenthal was one of the pioneers. In the 1980s, while researching how exercise helps patients with cardiovascular disease, he and his colleagues noticed an inadvertent secondary benefit: working out seemed to improve people's moods and reduce symptoms of depression. They decided to investigate. One of their early studies, published in 1999, tracked the health of 156 elderly men and women diagnosed with depression as they exercised regularly or took antidepressants, or both. After 16 weeks, all three groups had improved equally, but relapse rates were lowest among patients who exercised.

In a follow-up study, published a decade later, they divided more than 200 adults with depression into four groups, each receiving a different intervention: supervised exercise classes, exercise at home, medication or placebo. They found that patients engaging in supervised exercise fared better than those working out at home and achieved remission rates nearly equivalent to those of people taking antidepressants: 45 versus 47 percent, respectively. By comparison, the home exercise group reached a 40 percent remission rate and the placebo group 31 percent.

In a similar study in 2015, Swedish scientists assigned 946 patients with mild to moderate depression to one of three 12-week treatments: thrice-weekly sessions of yoga, aerobics or strength training; Internet-based cognitive-behavioral therapy; or standard counseling plus medication. Patients in all groups improved, but those engaging in exercise experienced the greatest benefits. Internet-based therapy came in as a close runner-up, but the typical treatment plan lagged behind both alternatives.

To date, numerous meta-analyses have kept score on the accumulating data. They do not all agree: a few have found no indication that exercise is helpful or have found that it offers only very small effects or greatly diminished benefits in the long term. But most have reached similar optimistic conclusions. A 2013 review by the nonprofit organization Cochrane, regarded as a leader in evidence-based medicine, concluded that exercise is just as effective a treatment for depression as medication and counseling.

A meta-analysis published in 2016 echoes Cochrane's finding. A team of international researchers examined 25 of the most rigorous experiments and determined that exercise, especially moderate to vigorous aerobic exercise under professional supervision, is indeed a potent treatment for depression. When they adjusted their analysis to account for weak studies—those most prone to some kind of experimental bias—they found an even stronger effect, suggesting that some previous meta-analyses may have underestimated exercise's benefits for mental health. The researchers further calculated that it would take at least 1,000 contradictory studies to negate the affirming evidence that has piled up so far. Yet another review computed that when exercise is

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GROUP EXERCISE offers the same physiological and psychological benefits as solo workouts plus social interaction, which can also ease depressive symptoms.

used to treat depression, success rates increase by as much as 67 to 74 percent.

HOW MUCH IS ENOUGH?

SOME RESEARCHERS have attempted to figure out what types of exercise and intensity levels are most effective as an antidepressant. In a frequently cited study from 2005, for example, Trivedi and his colleagues tracked the health of 80 adults with mild to moderate depression for three months as they exercised three to five times a week on a treadmill or stationary bicycle at low intensity (seven kilocalories per kilogram per week) or at a higher intensity, as recommended by public health authorities (17.5 kilocalories per kilogram per week). At the end of the three months, the adults who exercised at the higher intensity had lessened the severity of their depression by 47 percent, compared with only 30 percent for the low-intensity group and 29 percent for a group who engaged in stretching rather than aerobic exercise.

On the basis of studies such as this one, some psychologists, clinicians and health authorities have gone as far as publishing specific recommendations. Trivedi prescribes three to five 45- to 60-minute sessions of aerobic exercise (walking; running; cycling; or using a treadmill, stationary bike or elliptical trainer) each week at an intensity of 50 to 85 percent of maximum heart rate. "The ideal is probably at least 16 kilocalories per kilogram of body weight, which works out to 1,200 to 1,500 kilocalories each week for average body weight," Trivedi says. "If you can talk to your spouse on the phone, you're not working out at the right intensity."

Likewise Central Queensland University exercise psychologist Robert Stanton advises 30- to 40-minute sessions of aerobic exercise—walking, cross-training or stationary cycling—three to four times a week at low to moderate intensity for at least nine weeks. And the U.K. National Institute for Health and Care Excellence advocates group-based physical activity programs for patients with mild to moderate depression consisting of at least three 45-minute sessions a week for at least 10 weeks.

Other experts, however, think it may be too soon to get so specific. A 2013 review paper, for instance, concluded that both cardiovascular and resistance exercise, either alone or in combination, are effective at treating depression but that there are not yet enough data to definitively favor one form of physical activity over another. "Which exercise has the best mood effects, and what intensity is best? Does it work better alone or combined with other treatments? We don't know for certain yet," says psychologist Michael Otto of Boston University, who has studied both the emotional and cognitive benefits of exercise. "We can make some general suggestions, but we still need more data to be confident about the specifics."

WHY EXERCISE WORKS

IN THE PAST TWO DECADES scientists have uncovered numerous details about how exercise alters the brain, and the body as a whole, in ways that alleviate and protect against depression. The second you start running, pedaling or lifting a dumbbell, your body's chemistry begins to change. Exercise boosts your heart rate, sending blood, oxygen, hormones and neurochemicals surging through the body. In the moment, the body responds to exercise as a kind of stress—but it is ultimately beneficial. Some evidence suggests that habitual moderate exercise rewires the brain and immune system to better cope with physical and mental strain. The better the body becomes at dealing with stressors of all kinds, the lower the risk of a depressive episode. In fact, many researchers think of depression as a disorder of managing stress.

Exercise also seems to mimic some of the chemical effects of antidepressant medication. Based on increasing evidence, some scientists argue that certain cases of depression result from the impaired growth of both brain cells and the connections between them. Studies have documented the atrophy and loss of neurons in brain regions such as the amygdala, hippocampus and prefrontal cortex in patients with major depression. Antidepressants that increase levels of serotonin and other neurotransmitters might work by reinvigorating neural proliferation, a process that depends in part on a molecule called brain-derived neurotrophic factor (BDNF). In studies with both animals and people, exercise enhances the production of BDNF.

In one 2001 study, for example, rats given an antidepressant and the opportunity to run produced higher levels of BDNF compared with animals that only ran or only received medication. Moreover, they were better at enduring a stressful experience, swimming for longer in an inescapable water tank before giving up—a test designed to approximate the onset of depression. In an analogous human study in 2016, researchers in Brazil divided 57 adults taking the antidepressant sertraline for moderate to severe depression into two groups: one attended four sessions of aerobic activity a week for 28 days, and the other did not exercise. Symptoms abated similarly in both groups, but the exercise group improved on lower doses of antidepressants. The authors suspect that exercise enhanced the biochemical effects of

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the drugs. Similar studies have shown that simply recommending healthy lifestyle changes, such as establishing better sleep routines and getting more exercise, can dramatically boost the efficacy of antidepressants from a mere 10 percent remission rate with the drugs alone to a 60 percent remission rate.

And in a small but intriguing 2015 study, physician Helmuth Haslacher and his colleagues at the Medical University of Vienna in Austria compared the mental health and genomes of 55 elderly marathon runners and endurance bicyclists with those of 58 nonathletes. Among the nonathletes, they found a statistically significant correlation between the number of depressive symptoms these individuals experienced and a particular gene variant that interferes with normal BDNF production. Among the athletes, however, there was no such correlation. The researchers concluded that by stimulating BDNF production, long-term, vigorous aerobic exercise might actually counteract a genetic susceptibility to depression.

Neurobiology may also explain why, in addition to exercise countering depression, the inverse seems to be true: correlations in epidemiological surveys suggest that physical inactivity, while sometimes the result of depression, may also be a major risk factor for subsequently developing it. In a 2014 study of more than 6,000 elderly U.K. citizens, the more time people spent watching television, the more likely they were to report symptoms of depression (although this was not true for other sedentary activities such as reading). Those who participated in some form of vigorous physical activity at least once a week experienced less depression. Likewise, a 2015 survey of nearly 5,000 Chinese college students found that the more time a student spent in front of a TV or computer screen, the more likely he or she was to have depressive symptoms. In contrast, the risk for depression dropped the more physically active a student was, regardless of age, gender or residential background. A meta-analysis of 24 studies involving a total of nearly 200,000 participants reached the same conclusion: sedentary behavior was associated with an increased risk of depression. On average, active people are 45 percent less likely to be depressed than inactive people, according to the U.S. Office of Disease Prevention and Health Promotion.

SOURCE: JENNIFER CARTER

THE FEEL-GOOD FACTOR

BEYOND THESE physiological reasons, many social and psychological factors help to explain why working out can alleviate symptoms of depression. In comprehensive interviews, people who have struggled with the disorder say that exercise energizes them, gives them a sense of purpose and achievement, elevates their self-esteem and mood, regulates appetite and sleep cycles, and distracts them from negative thoughts. For those who exercise in a group, it can also provide a welcome opportunity for social interaction.

First, though, many people with depression must overcome a severe lack of motivation. "We need to educate people and give them tools to help monitor their progress," Trivedi says. "We make patients log in and communicate with us. If we find out they have skipped a day, we work with them to solve the problem and make sure that by the end of week, they complete their regimen." Jennifer Carter, director of sport psychology at the Ohio State University Wexner Medical Center, has come up with a bevy of practical tips. Among them: "Notice the facts," she advises. "For example, there are 1,440 minutes in a day. Perhaps you can find 30 of those to exercise." [*For more of Carter's suggestions, see box above.*]

Looking for Motivation? Remember These TIPS

10 minutes of exercise is better than none.

Set yourself challenging but realistic goals.

If you aren't exercising at all, start by taking the stairs instead of the elevator, or call a friend to schedule a walk once or twice a week.

Identify what motivates you: if you are competitive, join a recreational sports league; if you are a social butterfly, join an exercise class; if you are a nature buff, go on a hike.

Getting over that initial hurdle of low motivation seems to depend in particular on how much satisfaction and self-agency people experience while working out. "Enjoyment is fundamentally linked to how much people stick with exercise," Otto says. "I want them to do what is most fun and entertaining, whatever that might be." Research suggests that exercise as therapy succeeds when people choose the type and intensity. Most people prefer a moderate intensity, around or just below the ventilatory threshold—the point at which breathing becomes noticeably labored. In 2011 Patrick Callaghan, now at London South Bank University in England, and his colleagues asked 38 women with depression to exercise on treadmills in small groups three times a week, at either a prescribed intensity or one they personally selected. After a month, the women who chose how much to exert themselves had lower levels of depression and higher self-esteem compared with the other group.

Despite the mounting evidence that exercise can remedy some forms of depression, skepticism persists in academia and health care, Trivedi notes. "There is this general bias that exercise is not a bona fide treatment—it's just something you should do in addition to treatment, like trying to sleep and eat well," he says. "Even though recognition of exercise as a treatment is increasing," only some health insurance companies pay for gym time, he explains, and when they do, they often offer small temporary discounts. "I can prescribe a drug that costs $200 and insurance will pay, but they won't give $40 to open a gym membership."

Patients will need to change their thinking as well. "It can be hard for patients to think of exercise as a form of treatment," Otto comments. "We usually exercise to look good at the beach, to lose weight." Most individuals do not understand the degree to which exercise can reshape their mood, too. "Even if you feel like pulling in and doing nothing, exercise pushes you out," he adds. "Depression makes you feel like everything you're about to do is useless and pointless. That's exactly what exercise fights—you have to get up and go." SA

Ferris Jabr is a contributing writer for *Scientific American* and was a contributing editor for *Scientific American Mind*. He has also written for the *New York Times Magazine*, the *New Yorker* and *Outside*.

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OPINION

How I Broke the Cycle of Stress

A technique called goal diversification turns out to be surprisingly effective

By Ashten Duncan

MOST OF US CAN LIKELY RELATE TO THIS EXPERIENCE: you put all that you have into your work for prolonged periods and feel physically and mentally exhausted by the end. This common phenomenon is known simply as stress, a natural reaction to facing increasing demands without the necessary resources to meet them. In moderation, stress on our bodies and minds can elicit beneficial responses that enhance well-being, such as increased memory formation. As most of us know, however, there is often an imperceptibly fine line between advantageous stress and toxic stress from being exposed to too much for too long. Sadly, we often cannot control the balance between the two.

Whether it is on social media or our go-to news channels, we hear a lot about stress and deteriorating well-being in the U.S. In fact, this reality has become so pervasive that some of us probably normalize much of it, writing off the downstream effects of stress as just part of modernity. For adults working in fields associated with above-average levels of psychosocial stress, a vicious cycle can manifest wherein unmitigated chronic stress breaks us down, drains us of our resilience, narrows our perception of what makes life worth living, and leaves us feeling hollow. This entire process is often encapsulated in a single word: burnout.

For some, burnout, schmurnout! Critics of this concept tend to point out how nebulous it sounds even when someone offers up the definition. A different, more integrated way of understanding the long-term effects of chronic stress on the whole person is a principle called allostatic load. Although a lot happens to our bodies when we experience prolonged stress, the central idea of allostatic load theory is that if you apply enough force for long enough on someone without destroying the person, you will fundamentally change the way they function and respond to future stressors, through a process called maladaptation.

As a medical student, I see this problem of maladaptation frequently in both trainees and trained physicians. Research reflects this trend in the alarming number of physicians who quit practicing medicine every year. I think it is because we are so deeply focused on trying to carry out a complex mission of providing care to patients. In our efforts to do this, we often focus on one large goal after another, not allowing ourselves to have much latitude. Whether it is taking a standardized examination or meeting documentation requirements, setting and pursuing less diverse goals in this way is problematic: any barriers to goal attainment will cause much more stress than they would if we had other irons in the fire.

Major news sources and professional organizations have cited emerging evidence of epidemic levels of burnout among physicians in the U.S. This problem is not unique to physicians, but there is perhaps a pronounced susceptibility in this population because of how purpose-discordant tasks such as navigating electronic medical records hinder progress toward meaningful goals such as direct patient care. Although much work is being done to streamline these systems-level processes, not enough is being done to examine what goals are not being achieved and why they exist on a cultural level.

Doing what is in the best interest of the patient is at the heart of the Hippocratic oath, which represents a major theme in physician culture. The oft-overlooked con-

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nection between personal well-being and quality of patient care has an empirical basis: physicians who experience chronic stress and burnout are more likely to make errors that result in disease, disability or death. What is ironic is that physicians who push themselves to deliver the best care possible may be doing so at the expense of this goal!

SO WHAT DO WE DO ABOUT IT?

WE ARE MAKING STRIDES toward rectifying issues ingrained in our health-care systems, but progress toward shifting the culture to uphold our mission of optimal care is less robust. Research in positive psychology and organizational dynamics has shown that goal diversification is associated with subjective well-being. This means that the act of setting and pursuing different kinds of goals that are meaningful to you is associated with less stress, which decreases the impact of allostatic load on the body and mind. Studies on intervention strategies to promote goal diversification have included mindfulness meditation, hope building and active self-reflection exercises.

Hope theory describes how thinking about our motivation and perceived capability of attaining a goal and about the pathways leading to that goal influences how we set and go after what is important to us. It also suggests that goals, especially smaller ones, can serve as pathways to other, larger goals. This theoretical framework is further supported by research showing that goal setting promotes behavioral change, which can improve well-being even in the context of major depression. Moreover, the act of setting goals, particularly those that are diverse and of high personal value, increases productivity at work, which may subsequently help alleviate stress by decreasing the demands of one's work environment.

One of the most significant hurdles in health care is that clinical practice generally has a substantial workload and numerous legal constraints that force clinicians to stick to a script. So if the current practice environment largely opposes personal goal setting and goal diversity, how do we work around this? National research on health-care quality offers some ideas: decreasing daily workplace activity, adopting collaborative care models and allowing employees to work on quality-improvement projects. A common thread in all of these ideas is that health-care providers can focus on more than just the same repetitive goals, which allows them to feel that they are fulfilling their professional purpose more often. Additionally, this method can limit stress and prevent much of the maladaptation that comes with it.

People can break their cycles of stress and even flourish outside of the work they regularly do by incorporating new and different goals in their day-to-days. Our best shot at getting ahead of the problems stress produces is to look at where our finite energy is going and ask the tough questions: Why? At what cost? We are not machines; it is not sustainable for us to push ourselves at the cost of our well-being. Whether it is in medicine or any other field, we must ensure that our cultures nurture goal diversity and allow us to be more than just our work because, at the end of the day, stress occurs when we feel that we lack the resources to meet the demands around us. SA

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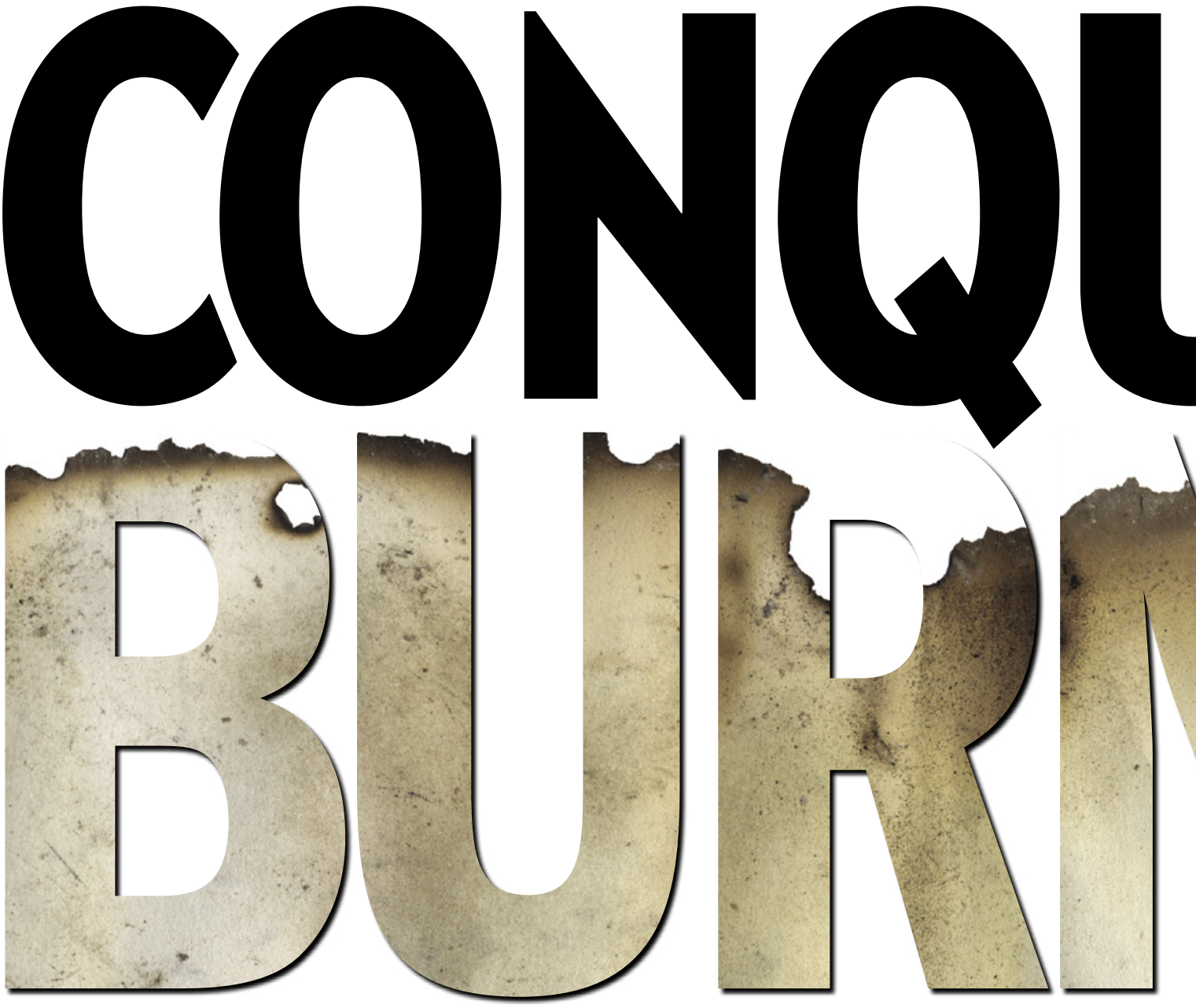

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JERING

Job satisfaction is a surprisingly fragile state. Here's how to protect yourself against the top contributors to burnout

By Michael P. Leiter and Christina Maslach

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You lie in bed in the morning, reluctant to swing your legs out from under the warm embrace of your blanket. After several bleary minutes, you finally rouse yourself, throw on some clothes and head to the office. Having arrived at your desk, you stare blankly as e-mail loads on your screen. When you first started this job, you derived deep satisfaction from addressing the day's challenges efficiently and artfully. Yet the optimism that used to buoy you is long gone. Now your morning coffee gives you the only jolt of energy you'll feel all day. The details differ by profession, but this state of being is the essence of burnout. It undoes a person's ability to pursue a happy, healthy and productive professional life.

Given that many of us spend the bulk of our waking hours at work, burnout can pose a real threat to overall well-being. Often it begins with pure exhaustion. When you are worn out, you invest less in your job. As a result, you accomplish fewer things and feel less effective than you did before. Because work has ceased to offer the same psychological rewards, you start to feel cynical about your role. This set of emotions—exhaustion, feelings of inefficacy and cynicism—feed off one another, producing a vicious cycle of deepening burnout.

So do you just quit? Quitting is probably not the answer, although you might want to look for a different job. To recover a professional joie de vivre, it helps to understand the basics of burnout from a psychological perspective. Decades of research have revealed several core truths about the syndrome. First, banish the idea that it arises from a personal failing. People who face burnout do not lack some essential quality such as work ethic, resilience or self-confidence. When all goes well, we naturally tend to bring dedication and pride to our work. Burnout represents the erosion of these noble qualities. Research has consistently pointed to management practices and poor job designs as the leading causes. The ways supervisors lead, and the structure of employees' workdays, fail to bring out the best in people.

If you suffer from burnout, your relationship with your job has gone sour. Just as a fight with a partner or close friend can exhaust you and cause you to pull away from that person, so can a soured relationship with your job sap your enthusiasm and alienate you. Relationships are complicated things, however, so there is no single solution, no magic bullet, no "one size fits all" approach. Yet with patience and optimism, anyone can find a path back to engagement.

THE RISE OF BURNOUT

The use of the term "burnout" began gaining popularity in the 1970s, especially among people working in human services. Herbert Freudenberger, a psychologist at an alternative mental health agency, and one of us (Maslach) wrote early articles describing idealistic young professionals in health care and social work who were overextending themselves. They felt discouraged because they did not have sufficient resources to do their jobs well. Instead of building a better world, they felt they were marking time in a dysfunctional system.

The global pandemic that began in 2020 disrupted work life, increasing the intensity for some while decreasing the intensity for others. Everyone was affected. Imposed changes to work, such as shifts from meeting in person to online meetings, classes or interviews, can weaken a person's sense of efficacy. In addition to workload, responding to disruptions in itself drains energy. Concerns about personal safety can increase cynicism. An understandable rise in the dimensions of burnout need not endure, but it is essential that employers support employees as they manage these disruptions to their work life. With experience, people adapt to change, learning ways to create a fulfilling life at work.

Based on research evidence accumulated over several decades, in 2019 the World Health Organization (WHO) defined burnout as "a syndrome conceptualized as resulting from chronic workplace stress that has not been successfully managed. It is characterized by three dimensions: feelings of energy depletion or exhaustion; increased mental distance from one's job, or feelings of negativism or cynicism related to one's job; and reduced professional efficacy." The WHO also stated that it recognized burnout as an "occupational phenom-

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enon" and declared emphatically that "it is not classified as a medical condition."

Ultimately the true culprit is a mismatch between a person and the circumstances of a job. You might not have the resources you need, or your bosses might expect you to complete a task in a way that clashes with your principles. For example, health-care providers in our surveys often cite tensions between their professional ideals—to be emotionally supportive to their patients—and the constraints that undermine that goal, namely, insufficient staffing and outsized workloads. The quantity of work is important, but the real trouble arises from an employee's perception of his or her performance.

Another type of mismatch stems from lack of control. Letting people make decistions about how they spend their days is vital to a healthy work arrangement, but a sense of control can be easily eroded. Managers who set unrealistic expectations for an employee contribute to attrition. So do colleagues who do not communicate well. We all rely on others while doing our jobs, and poor communication can make our workdays more difficult and unpredictable than they need to be. When people feel they lack control over their own work, they are particularly prone to feeling cynical and ineffectual.

Bosses who fail to express their appreciation also contribute to workers' feelings of inefficacy. Indeed, we have found in our research that negative interactions with a supervisor incline a person toward burnout. Yet not all praise is created equal. We worked with one organization in which employees resented an employee-of-the-year award. The rank and file perceived the accolade as an indicator of who was in the good graces of company leaders and little else. Seemingly inequitable promotions can similarly harm engagement. In a 2014 survey that one of us (Leiter) conducted of people's feelings of burnout, one respondent wrote, "It is difficult to watch the randomness of why some are promoted and others are ignored. It drains the spirit from you." That interviewee directly linked a feeling of being unappreciated with a loss of energy—a strong indication of burnout.

EARLY WARNING SIGNS

THE EMOTIONAL DISTRESS of this syndrome can persist for years. Because it can become chronic, we grew interested in discovering whether we might predict—and thus potentially ward off—the emergence of burnout. In a study published in 2008, we surveyed 446 employees of an administrative department at a large university, first at the beginning of our investigation and again a year later. We probed numerous areas of their work life to assess burnout. We were curious to see how people who scored high on one dimension—say, high cynicism or high exhaustion—would rate a year later. If they became more burned out, we wanted to know what tipping point might have sent them in that direction.

As it turned out, we found one such indicator: workplace fairness. People who perceived favoritism, cheating or other inequities were more likely to be burned out by the end of our study. Conversely, employees who viewed the workplace as a just environment tilted back toward engagement. A fluke event during the year of our study brought the issue of fairness into stark relief. Investigators uncovered department members who were stealing from their workplace. Our final survey occurred soon after a few employees were apprehended and dismissed, so we could assess how disruptive this event had been. The thefts undermined trust among colleagues, weakened employees' sense of job security and, as a result, deepened burnout.

Recent developments have distinguished burnout from other distressed states. Our research has identified three profiles in addition to the distressed "burnout" profile (exhaustion, cynicism, inefficacy) and its opposite, the positive "engaged" profile (energy, involvement, efficacy). The "overextended" profile seems similar to burnout in its high exhaustion level but differs importantly by having lower levels of cynicism and inefficacy. The "disengaged" profile, in contrast, has high levels of

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cynicism but relatively low levels of exhaustion and inefficacy. People in the "ineffective" profile feel energetic and involved but lack a sense of professional efficacy.

These distinctions matter. Research revealed that people in the overextended profile had one overriding concern: work overload. They gave every indication that with effective help managing their workload, they would move toward the engaged profile. In contrast, people in the burnout profile had many concerns beyond work overload, such as control, community, reward and fairness. They seriously doubted any alignment of their workplace values with their personal or professional values. Making a difference for them would be a much bigger job. A more precise definition of the problem can facilitate more effective solutions.

THE SOCIAL SOLUTION

BECAUSE BURNOUT DEPENDS HEAVILY on the specific relationship between person and job, broad guidelines for recovery are hard to come by. Nevertheless, we now believe that improving the quality of workplace relationships may be one general way to intervene. Social exchanges between colleagues play a role in many facets of burnout.

As you might expect, people share more readily with individuals they admire and trust. Conversely, hostile workplaces eat away at a person's ability to focus on his or her work. Consider, for example, this anecdote, also from Leiter's 2014 survey, in which one person articulates the energy tax of negative interactions: "I love my work. I am an avid learner and a very positive person. But I work in a toxic workplace. This is a highly political environment that encourages competition between colleagues, backstabbing, gossiping and hiding information. I find going to work very difficult and come home exhausted." Other participants in our studies have similarly cited the emotional toll of unpleasant interactions. They describe feeling upset for days following a few rude words from a colleague and losing sleep over the incident—both factors that make it difficult to engage in what otherwise might be pleasurable tasks.

An opportunity to alleviate burnout arose in a meeting with leaders of a hospital in 2016. These executives had taken reasonable action to strengthen the sense of community in struggling work groups, including by changing team leaders and reassigning or dismissing identified troublemakers. Managers had brought in inspirational speakers and conducted team-building exercises. All of this effort met with minimal success.

To tackle this problem, Leiter and his research team built on

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their previous work on work-group-based civility programs to develop a new method called SCORE (Strengthening a Culture of Respect and Engagement). This focused process, occurring over five sessions, delivers a structured curriculum. The Leiter team's previous research had demonstrated that guiding work groups to reflect on their social encounters can improve civility, with the downstream benefit of alleviating burnout.

Knowing that burnout has a social angle, we deployed a work-group civility process in several units of the hospital. Some of these units had a long history of problems, others were uncommunicative, and some functioned well but aspired to collaborate more. Employees were divided into groups of 15 to 20 people from their same unit. With larger units, we offered the sessions multiple times. A professional facilitator from a local consulting firm facilitated the sessions, with assistance from a co-facilitator who was an employee of the participating organization.

Before we began, we surveyed all our participants on their perceptions of civility in their unit and on their own conduct so that we could compare their impressions at the beginning and the end of the program. We also assessed the dimensions of job burnout.

Over two or three months the teams met five times with three weeks between sessions. The facilitator started off the first session by asking, "How do we show respect (or disrespect) for one another here?" Then attendees practiced enacting civil exchanges, showing acceptance, acknowledgment, appreciation and accommodation of one another. Later sessions addressed responding to incivility, as well as promoting civility within their work groups.

The meetings gave employees a chance to work through strained relationships and engage in more productive ways of defusing emotions. Between sessions, workers practiced specific civility behaviors and tallied acts of kindness they witnessed.

The project has continued in other health-care settings, as well as in financial institutions, a radio station, and police and fire departments. The research on work-group-focused civility programs over the past decade confirms that they bring improvements in both workplace civility and burnout. Implementing the program across a variety of settings identifies the mechanisms that help work groups free themselves from dysfunctional social dynamics.

The SCORE approach reflects actions that arise from considering burnout as a relationship problem. Social encounters with colleagues, especially with supervisors, create points at which the work-group culture becomes personal. Infusing these encounters with respect inspires energy, involvement and efficacy—the opposite of burnout.

FINDING ENGAGEMENT

GIVEN THAT NOT EVERY COMPANY is about to start implementing SCORE, what is an individual worker to do? Many corporations may see squeezing every bit out of employees to be to their advantage. Organizations by and large do not expect to retain their employees forever, so they are unlikely to serve their workers' long-term interests. Employees thus must shoulder the responsibility of maintaining a sustainable work environment.

How employees define their relationship with work gives us insight into their larger aspirations for work. How much control do they desire, knowing control brings accountability? Is being fully involved in a vibrant workplace community essential? Most centrally, what are the core values that define a meaningful work life? In other words, establishing a fulfilling relationship with work becomes more likely for people who know what they are seeking. Such insight allows people to make their case.

Because burnout is a relationship issue, the individual has some, but not complete, control over circumstances. What follows are a few basic strategies for improving your contribution to the relationship. The good news is that many of these suggestions happen to be good for life in general, so you will benefit in many ways from developing these habits.

First up is fitness. A healthy way of life increases your resilience. A combination of sufficient exercise, nutrition and sleep will reduce your vulnerability to exhaustion. Although the job will not change, you will increase your endurance—and maybe even learn to thrive.

Closely related to fitness is a habit of integrating recovery cycles into your life. Demanding work depletes your physical, emotional and cognitive resources. As the saying goes, there is a reason it is called work. Your personal life should afford opportunities to enjoy relationships, catch up on sleep and take time for reflection. To reverse a trend toward burnout, a key step is to establish a firm structure for recovery activities. Lacking a structure, you will not make time for recovery in the course of a busy life.

You can incorporate small amounts of exercise and recovery into the workday, too. The strategy here is simple: get off your butt. Set an alarm every 30 minutes as a signal to get up and walk around. You can devise some activities that would convince an observer that this meandering is a necessary part of your work.

Now let us incorporate the social angle. As we demonstrated with SCORE, improving the quality of day-to-day exchanges among colleagues reduces burnout. You do not need your entire team to join you on this journey, but if you can recruit a friend or two to share a burnout-reduction project (a short midday walk, perhaps) the mutual support can be powerful.

Receiving good vibes from others is an uplifting experience, but so, too, is expressing them to others. Keep a tally of your own acts of kindness toward colleagues. To whom did you express appreciation today? Collaborating with a companion will, again, help you get the most out of this project.

Last, consider job crafting. You very likely have more latitude in your work than you think. Job crafting is an analytic approach that involves identifying the duties you find tedious and the aspects you find fulfilling. You should develop a plan to spend a bit more of your day on the good parts. Those increments can add up over time. Just ensure that the additional time you are spending on the fulfilling tasks makes a meaningful contribution, so as to keep your colleagues and supervisor onboard.

These ideas may sound like a big investment, but the truth is that burnout can be hard to shake. Once the syndrome has set in, you must commit to a deliberate practice to find your way back to a healthy, fulfilling relationship with work. Yet it can be done, so let's get started. SA

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GIVE ME A BREAK

A wealth of psychological research shows that mental downtime is vital for productivity and health. Some employers are finally starting to listen

By Ferris Jabr

Illustrations by RADIO

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THE MOMENT THAT INCITED MARK BERTOLINI'S WORKPLACE REVOLUTION DID NOT happen in the office, at a conference or even when he was thinking about his job—it occurred during a family vacation. But it was not a happy moment; in fact, it nearly killed him. In February 2004 Bertolini, then 47 years old, was on a skiing trip with his family in Killington, Vt. While speeding downhill, he collided with a tree and fell 30 feet down a ravine. The plummet fractured bones in his neck and back and severely damaged nerves in his arm. Yet he lived, gradually regaining mobility despite chronic pain. Not wanting to remain on pain medications for the rest of his life, he turned to yoga and mindfulness meditation, which teaches people to observe their thoughts, feelings and perceptions as they arise without judgment or resistance.

He was so impressed by these pain- and stress-reducing therapies that he started to wonder whether his 50,000 employees might benefit from them, too. At the time, Bertolini was chief executive officer of the health insurance giant Aetna.

By 2010 Bertolini had enlisted the help of the American Viniyoga Institute and meditation instruction company eMindful to customize free yoga and meditation classes for Aetna employees, even providing spaces at the office to practice. And he did not stop there. He also teamed up with health psychologist Ruth Wolever, then at Duke University and now at Vanderbilt University, to formally investigate the outcomes of these innovations.

In a three-month study of more than 200 Aetna employees, individuals who engaged in meditation and yoga slept better, felt less stressed overall and had more efficient heartbeat recovery rates after stress than those who abstained. In a follow-up study involving more than 1,000 employees, presented in May 2016 at the International Congress of Integrative Medicine and Health, meditation and yoga were correlated not only with less stress but also with 47 to 62 minutes of increased productivity per week. The practices even seemed to reduce employees' spending on health care. (The studies were funded in part by Aetna and eMindful, but all were reviewed by independent committees at Duke.) "The first year after we did the program, our health-care costs actually dropped as a company," Bertolini wrote in an e-mail. He attributes some of Aetna's subsequent success and growth to the new practices.

The programs were so successful and popular that in 2016 Aetna brought on mindfulness instructor and consultant Andy Lee as its full-time chief mindfulness officer—presumably the first position of its kind in the country. "In today's workplace, we all have more information than we know what to do with, and people are always asked to do more with less," says Lee, who has since left Aetna. "That taxes our minds and our bodies. Dedicated time for rest and relaxation is an ideal countermeasure."

Around the world, especially in industrial nations, overworked employees and the scientists who study them are reaching similar conclusions. A preponderance of evidence now confirms that downtime of all kinds—whether it be a meditation session, a lunchtime stroll through the park or a weeklong vacation—is crucial for productivity and overall health. When we are relaxing or daydreaming, the brain does not slow or stop. Rather—much as an array of crucial molecular, genetic and physiological processes transpire during sleep—many mental processes require periods of waking rest during the day. Downtime restores attention and motivation, fosters creativity, improves work efficiency, and is essential for us to both achieve our highest levels of performance and simply make it through the day.

UNDER PRESSURE

PSYCHOLOGISTS began formally studying the health and habits of workers during the first decades of the 20th century. Pioneering workplace psychologist Walter Dill Scott, elected president of the American Psychological Association in 1919, focused on how best to choose employees with the most appropriate skills. In the early 1900s Hugo Münsterberg published the first textbooks explicitly focused on human behavior in the workplace, a field that is now variously known as industrial/organizational, occupational or, simply, work psychology.

Although the field has long been interested in the relations among stress, rest and productivity, it was not until the 1980s

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and 1990s that topics such as work-related fatigue, mental breaks and work-life balance received widespread attention. In the past decade the number of studies on such issues has increased dramatically.

Researchers identify several reasons for this new emphasis, such as the growing number of couples and families in which both partners are managing full-time careers, as well as the rising prevalence of white-collar desk jobs in which the psychological toil of work takes precedence over the kind of physical repercussions associated with hard labor. But the biggest impetus is probably the advent of technology that makes it possible to keep working 24/7 and remain in touch with colleagues even when far away from the office. "We've created a culture of immediate responsiveness," says Leslie A. Perlow, a professor at Harvard Business School. "It's getting to the point where thanks to mobile devices we can work from anywhere, and we can interrupt one another anytime."

Studies confirm that many modern employees, especially in the U.S., are perpetually preoccupied with work: even when they get a break, they feel obligated to keep working. The European Union mandates 20 days of paid vacation, but the U.S. has no federal laws guaranteeing paid time off, sick leave or breaks for national holidays. Canada, Japan and Hong Kong mandate just 10 or fewer days of annual vacation; in the U.S., workers receive an average of just eight days after one year on the job. But a 2014 survey by Harris Interactive found that we use only half of our eligible vacation days and paid time off. A 2015 report by Expedia showed that Americans collectively neglect 1.3 million years of vacation annually. And in several surveys, U.S. workers have confessed that they do not fully unplug from their phone or e-mail even when they are on vacation or sick leave.

Larissa Barber, now a psychology professor at San Diego State University, and her colleagues coined a new term for such feelings: workplace telepressure, a nagging preoccupation with work-related e-mails and related communications, combined with a compulsion to respond immediately. "All of this is tied to the American culture of busyness," Barber says. "Being busy means status and prestige, and if you are not busy and overwhelmed, it means you're not important or not working hard enough."

In a survey of more than 300 part- or full-time workers published in 2015 in the *Journal of Occupational Health Psychology,* Barber and her colleagues found that employees who reported greater workplace telepressure missed more days of work, experienced more physical and mental burnout, and did not sleep as well as their less e-mail-obsessed peers. Barber also suspects that telepressure can lower the quality of an employee's work. "Responsivity doesn't always mean productivity," she says. "All it shows is that someone is responding and available, but that is different from doing good work."

The increasingly intrusive nature of work-related communication is especially troubling in light of one of the strongest conclusions from the past decade of occupational psychology research: to maximize the benefits of breaks, we need to fully disengage from our jobs—physically and mentally. "No matter how we look at it, detachment is good for well-being," says Charlotte Fritz, an organizational psychologist at Portland State University, who published a review paper on the topic in 2015. "The benefits include lower exhaustion, higher positive mood, better sleep and better quality of life."

THE (QUALIFIED) CASE FOR MORE VACATION

PERLOW AND HER COLLEAGUES have conducted some of the most rigorous research on how uninterrupted downtime improves health and productivity. In one four-year study, she and her team monitored the work habits of employees at the Boston Consulting Group, who were used to working nearly nonstop. Every year the researchers insisted that employees take regular time off, even when they felt they should be in the office. In one experiment, published in 2009 in the *Harvard Business Review,* each of four consultants on a team took a break from work one day a week. In a second experiment, every member of a team scheduled one weekly night of inviolable personal time.

Everyone resisted at first, fearing that work would pile up. But the consultants gradually came to love their mandated time off because it restored their willingness and ability to work, making them more productive overall. After five months the study subjects were more satisfied with their jobs, more likely to see a long-term future at the company, more satisfied with their work-life balance and prouder of their accomplishments. These initial

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experiments were so successful that within four years, the Boston Consulting Group had implemented the same practices in more than 2,000 teams in 66 offices in 35 countries.

Collectively, studies by Perlow and other researchers suggest that the current model of consecutive 40-hour workweeks punctuated by two-day weekends and one or two vacations a year is not ideal for mental health or productivity. Psychologists have established that, like weekends and evenings, vacations have genuine physical and psychological benefits: they reduce stress, promote creativity and revitalize attention.

Yet a comprehensive meta-analysis published in 2011 by psychologist Jessica de Bloom, now at the University of Tampere in Finland, demonstrates that these benefits generally fade within two to four weeks. In one of her own studies, for example, 96 Dutch workers reported that compared with their typical daily experience, they felt greater energy and happiness, less tension and more satisfaction with life during a winter sports vacation between seven and nine days long. Within just one week of returning to work, however, all sense of renewal had vanished. A second experiment with four and five days of respite came to essentially the same conclusion.

A vacation is like applying a single ice cube to a burn: it will help for a little while, but soon enough the ache returns. The U.S. standard of two weeks' annual vacation time is nowhere near enough to sustain such ephemeral benefits throughout a given year because it allows for too few discrete breaks. And many people save up their scant vacation time to use all at once. "It's not necessarily true that longer breaks or holidays have better results," de Bloom says. "It seems that regularity is much more important."

Given the current work climate, the prospect of frequent breaks during which employees disconnect *completely* from their jobs may seem unlikely, but it is a much more pragmatic and affordable strategy than lengthy vacations. Baby steps involve curtailing job-related communications in the evenings and on weekends.

Some companies do set boundaries on work e-mail: in 2011, for example, Volkswagen prevented employees from accessing work-related e-mails on company-issued phones during nonwork hours. France and Germany have restricted after-hours work communication in certain sectors or situations. But such practices are the exception. In one 2012 survey, only 21 percent of organizations had a formal policy limiting use of work-issued mobile devices during off-hours.

On an individual level, Barber recommends strictly managing expectations. Replying too quickly often sets up unrealistic standards. On her class syllabus, she explicitly states when she is available to reply by e-mail and when she is not. Meanwhile de Bloom spreads her vacations as much as possible throughout the year. And her polite but firm out-of-office e-mail response cites studies on the benefits of mentally detaching from work during vacation.

HITTING REFRESH

WEEKENDS AND HOLIDAYS ASIDE, simple daily practices can allow employees to mentally detach from their desk work. Tony Schwartz, a journalist and CEO of the Energy Project, has made it his mission to advise people on implementing these practices. Building on the available science, his company provides coaching and consultations for organizations that want to help individuals avoid burnout and dissatisfaction.

The Energy Project instructs workers to get seven to eight hours of sleep every night, use every vacation day, take naps and other small breaks throughout the day, learn to meditate, and take on the most challenging projects first to give them maximum attention. Although their approach counters the reigning cultural conviction that busier is better, the organization has partnered with Google, Apple, Facebook, Coca-Cola and a wide range of Fortune 500 companies. According to Schwartz, their strategies have pushed workers' overall engagement well above average levels (as measured by self-reports of how much people

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enjoy their job and are willing to take on extra duties). Google maintained the partnership for more than five years.

More than a decade of research has uncovered the fact that although our mental resources gradually ebb from dawn to dusk, breaks can restore at least some of these cognitive faculties. Naps, for instance, can sharpen concentration and improve the performance of both the sleep-deprived and fully rested on all kinds of tasks. In a 2002 study, 26 physicians and nurses working three consecutive 12-hour night shifts dozed for 40 minutes at 3 A.M. while 23 of their colleagues worked continuously without sleeping. Although doctors and nurses who had taken a siesta scored lower than their peers on a memory test at 4 A.M., at 7:30 A.M. they actually outperformed their counterparts on a test of attention, more efficiently inserted a catheter in a virtual simulation and appeared more alert during an interactive simulation of driving a car home.

IN ONE STUDY, MEDITATION AND YOGA WERE CORRELATED NOT ONLY WITH LESS STRESS BUT ALSO WITH 47 TO 62 MINUTES OF INCREASED PRODUCTIVITY PER WEEK.

Some start-ups and progressive companies provide employees with spaces to nap at the office, but most workers in the U.S. do not have that option. Another restorative solution is spending more time outdoors, away from human-made spaces. Psychologist Marc Berman, now at the University of Chicago, studies the hypothesis that natural environments restore our attention. Built-up environments, such as crowded city streets, he argues, may overwhelm the brain with noisy, glaring stimuli, whereas the calm and quiet of green spaces, such as parks and forests, allow the mind to relax and recuperate.

In one of the few controlled experiments in this area, published in 2008, Berman asked 38 University of Michigan students to complete two attention-draining tasks: first studying lists of numbers and reciting them from memory in reverse order, then memorizing the locations of words in a grid. Half the students subsequently ambled along an arboretum path for about an hour, and the other half walked the same distance through busy downtown Ann Arbor. Back at the laboratory the students once again memorized and recited strings of numerals. On average, the volunteers who had spent their time amid trees rather than city traffic recalled 1.5 more digits than the first time they took the test; those who had walked through the city improved by only 0.5 digit—a small but statistically significant difference between the two groups.

CLEARING THE MIND

IN ADDITION TO ENHANCING one's powers of concentration, downtime can strengthen attention—something that scientists have gleaned through studies of meditation. In the past decade mindfulness training has become incredibly popular as a strategy to relieve stress, exhaustion and anxiety—especially for overworked nine-to-fivers (or nine-to-niners, as is often the case).

Critics of mindfulness research observe, correctly, that studies on the benefits of this practice are typically small and that they lean on subjective reports; the science of mindfulness is still not a rigorous one. Nevertheless, at this point researchers examining the benefits of mindfulness have gathered enough evidence to conclude that meditation can improve mental health, hone concentration and strengthen memory. Experiments that contrast longtime expert meditators with novices or people who do not meditate often find that the former outperform the latter on tests of mental acuity.

In a 2009 study, for instance, neuroscientist Sara van Leeuwen, then at Goethe University Frankfurt in Germany, and her colleagues tested the visual attention of three groups of volunteers: 17 adults around 50 years old with up to 29 years of meditation practice; 17 people of the same age and gender who were not longtime meditators; and 17 young adults who had never meditated before. These participants viewed a series of letters flashed on a computer screen, concealing two numerals in their midst. Volunteers had to identify or guess both digits; recognizing the second number was often difficult because earlier images masked it. Performance on such tests usually declines with age, but the expert meditators outscored both their peers and the younger participants.

Changes to the brain's structure and to behavior most likely explain these improvements. Over time expert meditators may develop a more intricately wrinkled cortex—the brain's outer layer, which is critical for many sophisticated mental abilities such as abstract thought. These practitioners may also have increased volume and density in the hippocampus, an area that is absolutely crucial for memory. Finally, meditation appears to thicken regions of the frontal cortex that we rely on to regulate our emotions and prevent the typical wilting of brain areas responsible for sustaining attention as we age.

At this point scientists are still unsure of how quickly these changes occur, although some studies suggest that a few weeks of meditation or a mere 10 to 20 minutes daily can sharpen the mind. But there is likely a catch: as with vacations, a few studies indicate that regularity is ultimately more important than the length of any one session. Just 12 minutes of daily mindfulness meditation helped to prevent the stress of military service from corroding the working memory of 34 U.S. marines in a 2011 study conducted by Amishi P. Jha, now at the University of Miami, and her colleagues. Jha likens mindfulness training to push-ups: as a mental workout, she says, "it's low-tech and easy to implement." In her own life, she looks for any opportunity to practice, such as her 15-minute daily commute.

Since Bertolini introduced mindfulness and yoga courses to Aetna, more than 13,000 employees have participated. "There's been this incredible trajectory in peer-reviewed work on mindfulness and related relaxation techniques in the workplace," says Wolever, the former Duke researcher who studied Aetna employees. "We need to work against that culture of always being busy and develop more realistic expectations of what our brains and bodies can handle." SA

Ferris Jabr is a contributing writer for *Scientific American*. He has also written for the *New York Times Magazine*, the *New Yorker* and *Outside*.

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BEING IN THE NOW

A focus on the present, dubbed "mindfulness," can make you happier and healthier. Training to deepen your immersion in the moment works by improving attention

By Amishi P. Jha

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PULLING INTO A PARKING SPOT AT WORK, YOU REALIZE YOU HAVE NO recollection of the drive that got you there. While reading a news story, you arrive at the bottom of the page, frustrated that you have no idea what you just read. In midconversation you suddenly become aware that you have missed what the person speaking to you has said.

These episodes are symptoms of a distracted mind. You were thinking about a project idea while driving, reliving a troubling memory while attempting to read, envisioning a weekend getaway with friends during a conversation with your co-worker. Whether the mind journeyed to the future or to the past, whether the thoughts that whisked you away were useful, unpleasant or pleasant, the consequences were the same. You missed the experience of the moment as it was unfolding. Your mind drifted into mental time travel.

AWAY FROM THE NOW

MENTAL TIME TRAVEL evolved to advantage our survival. By reexperiencing the past, we can learn from it, and by preexperiencing the future, we can prepare for it. Both *retro*spection (rewinding events in the mind) and *pro*spection (fast-forwarding them) rely on our brain's capacity for mental simulation. And based on the brain nodes and networks that carry out simulation, chief among them regions of the prefrontal cortex, we can glean that this is a recently gained evolutionary development. How does mental simulation work, and what does it have to do with stress and mind wandering (which is distinct from deliberate daydreaming)?

Before we discuss that, let's test our simulation abilities. Imagine being handed a delicious chocolate cupcake with creamy white frosting. You lift it up to your mouth, anticipating the rich chocolate flavor. But as you go to take a bite, I inform you that the frosting is made of cod-liver oil and cauliflower. The likely response: Yuck!

Let's break down what happened. The initial description of the cupcake prompted a mental image in your mind, and your attention transported you into a simulated experience, perhaps so vivid that you could almost taste the cupcake and feel your mouth watering. You recoiled as soon as you "pretasted" the seemingly disgusting cod-liver oil concoction.

Simulations have the power to transport our attention out of the present moment while simultaneously altering our cognitive, emotional and physiological responses in the now. The same mental powers that drove up your salivary response when you "previewed" a cupcake can drive down your mood, focus and thinking if you preview a threatening episode over and over. Worse, they can stimulate the pituitary gland to release more stress hormones. Herein lies the downside of this evolutionary advance: as our attention journeys to an alternative reality, our mind and body respond as if that reality were unfolding in the here and now.

Research suggests that this type of mental meandering away from our present moment has many deleterious consequences for our minds, bodies and relationships. Such mind wandering can spike during stressful times in our lives, be they acute or chronic events. And as mind wandering increases in the form of more frequent rumination or worrying, our experience of stress expands, creating a spiral of thinking

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1

MODERN MINDFULNESS practices have their roots in customs that have been integral to Eastern cultures for millennia.

2

LEARNING to be more mindful, or aware of what is happening now, is an antidote to rumination, worry and fear—and their effects on mental health.

that reduces our concentration while increasing our levels of stress hormones.

In my laboratory at the University of Miami, we study the human brain's attention system. To investigate whether and how stress influences attention, we partner with people in some of the most extreme, high-demand lines of work: medical professionals, firefighters, soldiers and elite athletes. They need to deploy their attention—and do it well—in extraordinarily high-stakes circumstances where their decisions could impact many people. One group we have worked with extensively is the U.S. military. Whether and how people in this demographic pay attention can be a matter of life or death. For all of us, attention is a powerful force that shapes our lives far more than we realize.

Our attention influences our perceptual, emotional, decisional and social functioning and therefore affects our sense of fulfillment and accomplishment. Many of our participants experience protracted high-stress intervals, such as soldiers enduring predeployment training or military deployment, and we wondered what happens to attention over these intervals. We learned that, similar to what is observed in lab-based studies, experiencing stress in the field indeed causes attentional performance to decline while increasing mind wandering. This prompted the next important question: Can attention be trained to resist stress-related increases in mind wandering?

My group first considered mindfulness training as a potential solution in the early 2000s. If mentally zooming into the past or future was the root cause of "attentional hijacking," then perhaps the most effective antidote would be a training regimen that emphasized a present-centered attentional stance.

ANTIDOTE TO A WANDERING MIND

THE OPPOSITE OF A WANDERING MIND is a mindful one. Mindfulness is a mental mode characterized by attention to the present moment without evaluation or emotional reaction to it.

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BY IMPROVING the ability to direct and monitor attention, mindfulness meditation could enhance people's performance in pursuits as diverse as sports and surgery.

Eastern cultures have proffered various forms of meditation as a solution to the conundrum of human suffering. Ancient texts detail precise training exercises to cultivate specific mental qualities. One form of meditation, which we now call mindfulness meditation, instructs practitioners to pay attention to ongoing perceptual experience rather than conceptual trains of thought. People have been engaging in mindfulness exercises for millennia, claiming improved mental clarity and calm—and even greater longevity.

Thousands of articles lay out evidence that training to become more mindful reduces psychological stress and improves both mental and physical health, alleviating depression, anxiety, loneliness and chronic pain [*see box on page 92 for a sample exercise*]. Many workplaces and medical centers now offer mindfulness-based programs to improve well-being. There has been an explosive proliferation of mindfulness training modalities beyond this as well, from apps and asynchronous online trainings to trainer-led in-person and remote programs.

One broad category of mindfulness exercises is focused-attention practices. These practices guide individuals to select a specific sensation tied to, for example, breathing and direct attention to that sensation. Instructions next encourage the practitioner to notice when his or her mind has wandered away from that attentional target and, when mind wandering is registered, to simply return attention back to the immediate breath-related sensations.

A second category emphasizes receptive-attention practices, which coach practitioners to engage in open monitoring. They are to watch what enters and then drops out of conscious awareness moment by moment. Think of hearing the faint sound of a fire truck's siren in the distance. The sound becomes louder as the truck approaches, then fainter again as it passes. You may notice that the siren is initially part of a vast sea of sounds and later the most salient sound, only to fade into the background again. Thoughts, emotions and other sensations may similarly grow and diminish as we remain in a watchful monitoring mode.

One of the best-studied mindfulness training programs was developed by Jon Kabat-Zinn of the University of Massachusetts Medical School in the late 1970s. The program, called mindfulness-based stress reduction (MBSR), introduces participants

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AMISHI P. JHA and Brigadier General (now Lieutenant General) Walter Piatt review brain-wave recording procedures, along with a memory test that military service members take before and after mindfulness training.

to both these broad categories of exercise. It is offered over eight weeks and involves weekly group meetings with a qualified trainer, as well as daily homework practices of 45 minutes a day.

As its name highlights, MBSR aims to promote stress reduction, as well as treatment for those suffering from any one of myriad ailments. The application and reach of MBSR have mushroomed over the past decade, and it has guided many mindfulness-based interventions (MBIs) designed to improve the health of the body, the mind and relationships. These practices have been shown to alleviate stress-related inflammatory and cardiovascular diseases, as well as psychological disorders and diseases such as anxiety and depression. In addition, several studies report that MBIs improve interpersonal dynamics and team cohesion in the workplace.

TRAINING ATTENTION

FROM A CLINICAL PERSPECTIVE, although the field is admittedly in its infancy, the evidence is promising regarding the somatic, psychological and social benefits of mindfulness training. Yet my interest is from a cognitive neuroscience perspective: If mindfulness does work, *how* does it work? A review of mindfulness training exercises showed that they certainly highlight attention, but they also emphasize the detection of mind wandering. We needed to put mindfulness to the test in a manner that would allow us to assess both these components.

To do this, we used the "sustained attention to response" task, or SART. This test was developed in the late 1990s, and, as the name suggests, it tests a person's ability to sustain attention. Participants sit in front of a computer screen where a number appears for half a second and then vanishes. A half-second later, another number appears and then vanishes, and so on for 20 minutes. Their job: press the space bar every time a number appears—*unless* the number is three. By design, the number three appears only 5 percent of the time.

This test engages the three main subsystems of attention: orienting, or directing attention; alerting, or noticing events; and executive attention, or managing goals and performance. You orient attention to the screen, focusing on each number as it flickers; stay alert for the appearance of the number three; and use executive attention to make sure you are following the instructions and pressing the key only when you should.

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It sounds simple, but it is not easy. Most participants do not perform well on this task. Why? They quickly go on autopilot, lost in their own mental simulations, and press the space bar no matter what number appears. Their attention goes off task. We know this because we stopped the experiment and asked them every now and then. Their minds wandered numerous times throughout the experiment, and during those episodes, their performance suffered compared with when they stayed on task.

We have used this experiment in many studies to see whether mindfulness training strengthens attention and reduces mind wandering in individuals experiencing intervals of high demand such as an academic semester or military deployment. We found that for a variety of groups ranging from undergraduate students to elite military units, mindfulness training indeed benefited SART performance. Compared with those who received no training, those in the mindfulness training groups had higher SART accuracy scores and less mind wandering over time.

In a 2020 study published in the *Journal of Cognitive Enhancement,* Frederikke Piil, then at the University of Southern Denmark, and her colleagues examined the consequences of acute stress and mindfulness training on SART performance in 48 university students and staff members. All participants were provided with one of two apps that required their engagement in daily practices over an interval of one month. One group used a mindfulness app to practice mindfulness exercises, and the other group used a cognitive training app to complete simple cognitive exercises.

To determine a baseline at the start of the experiment, participants first completed a cold pressor task—they submerged their nondominant hand in a tank of circulating ice water until it became too uncomfortable to keep it there. This task has been found to reliably increase stress as measured by increases in arousal of the sympathetic nervous system (for example, increased heart rate, blood pressure and stress hormones). Afterward they completed the SART. They returned a month later and once again completed the cold pressor task followed by the SART. Only the mindfulness group improved in their SART performance, and the more they used the mindfulness app, the more their performance benefited.

Because attention and mind wandering are known to correspond with academic performance, Clemens C. Bauer of the Massachusetts Institute of Technology and his colleagues used the SART test in combination with brain imaging in school-aged children. In their study, published in 2020 in *Human Brain Mapping,* half of 99 sixth graders received mindfulness training, and the other half received a computer-coding course.

After training, only the mindfulness group demonstrated preserved SART performance over the demanding academic semester. This group showed increased anticorrelation between activity in the central executive network, a key brain network for attention, and activity in the default mode network, known to be activated during mental simulations and mind wandering. Greater anticorrelation between these two networks after training indicates that only members of the

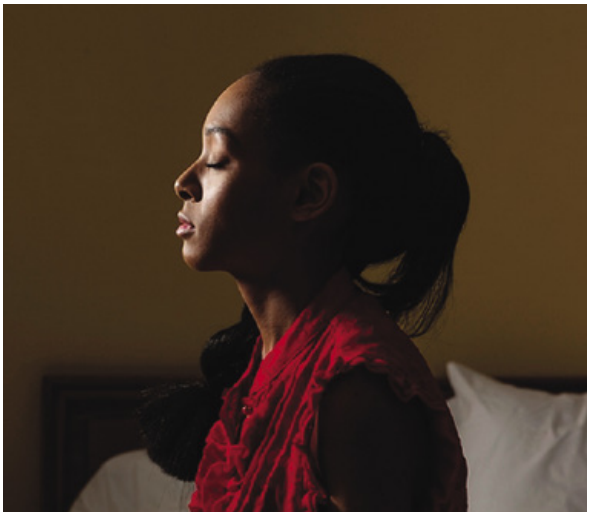
Capturing Attention

Mindfulness, a focus on the present moment without judgment, has proven benefits for health and happiness. Engaging in daily mindfulness workouts can help you assume this mental mode more often in your daily life. The following 10- to 15-minute mindfulness exercise is designed to train two types of attention: concentrative focus (a narrowing of attention and open monitoring) and a broad awareness of sensations and surroundings.

Here's what to do:

- Sit in an upright, stable position, hands resting on your thighs or cradled together.
- Lower or close your eyes, whichever is more comfortable for you.
- Attend to your breath, following its movement throughout your body.
- Notice the sensations around your belly as air flows into and out of your nose or mouth. You have been breathing all day—all of your life—and in this moment, you are simply noticing your breath.
- Select one area of your body affected by your breathing and focus your attention there. Control your focus, not the breathing itself.
- When you notice your mind wandering—and it will—bring your attention back to your breath.
- After five to 10 minutes, switch from focusing to monitoring. Think of your mind as a vast open sky and your thoughts, feelings and sensations as passing clouds.
- Feel your whole body move with your breath. Be receptive to your sensations, noticing what arises in the moment. Be attentive to the changing quality of experience—sounds, aromas, the caress of a breeze ... thoughts.
- After about five more minutes, lift your gaze or open your eyes.

—Scott Rogers, director of programs and training, UMindfulness Research and Practice Initiative, University of Miami



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mindfulness group improved in their cognitive control. These results suggest that mindfulness training may help children to stay focused and complete the task at hand.

Interestingly, recent work by Lukas Lenhart of the Medical University of Innsbruck in Austria and his colleagues in which participants received seven weeks of mindfulness training revealed altered brain structure in specific nodes tied to attention and mind wandering. In that study, published in 2020 in *Behavioural Brain Research,* 27 participants received an MRI scan before and after the mindfulness course. The researchers observed increased gray matter density in subjects' frontal lobe nodes within attentional networks, as well as decreases in gray matter density within nodes of the default mode.

Together these studies suggest that mindfulness training may provide a type of mental armor during times of protracted and acute stress and can serve to boost focus. It appears to benefit both children and adults, resulting in functional and structural brain changes. Such training allows us to break free from a wandering mind that can distract us from the task at hand and sour our mood. With our full capacity available to us, all aspects of our functioning that are fueled by attention will benefit, be it our ability to think, feel or connect.

PRESCRIPTION FOR THE BRAIN

EFFORTS TO BECOME MORE MINDFUL could make a considerable dent in human suffering. Working mindfulness practices into your daily routine may bring benefits similar to those of physical exercise. Indeed, as with physical exercise, mindfulness exercises are stress-protective, and the more you do, the more you benefit. As an antidote to an ambling mind, negative mood and stress, such mental workouts may have the potential to help virtually everyone live a happier, healthier and more fulfilled life. Students or athletes who want to boost their performance, for example, and parents, teachers or caregivers wishing to be more attentive to others' needs may all find mindfulness training useful. Such training may be particularly essential, however, for soldiers, first responders, critical care nurses and physicians, and air-traffic controllers, whose ability to control and monitor their attention may be a matter of life or death.

A key insight from our research is that merely learning about the damaging effects of stress or the benefits, history or mechanisms of mindfulness training did not lead to attentional improvements. Only engaging in regular mindfulness practice did. In studies across military service members and athletes, among others, we found a dose-response effect; the more practice people engaged in, the more they benefited. But conversely, we also found that when we assigned 30 minutes of daily practice, most time-pressured participants simply did not comply. Some did the 30 minutes; others did none. We pursued this "dosing question" across several studies to arrive at a daily practice prescription to which participants were willing to adhere: 12 to 15 minutes a day five days a week. When this group followed through, we saw beneficial effects on their attention. The research continues, and many more studies will be required.

With evidence of its benefits mounting come new challenges for mindfulness training. How can access be scaled up *and* meet the needs of specific groups? Based on our past research, my colleague Scott Rogers and I created a short-form program called mindfulness-based attention training (MBAT). Once we found the core program to be effective, we developed train-the-trainer methods to address scalability challenges. MBAT's modular structure and exercises allow for flexibility so the program can be customized for a variety of groups, from soldiers to medical students, athletes, business professionals, first responders and teachers. The linchpin of the program's success is the competency of the trainers. We are finding that more so than prior expertise in mindfulness, successful trainers must have familiarity with the cultural norms, sensitivities and stressors that a particular community faces.

MINDFULNESS TRAINING MAY PROVIDE A TYPE OF MENTAL ARMOR DURING TIMES OF PROTRACTED AND ACUTE STRESS AND CAN SERVE TO BOOST FOCUS.

The scientific literature on mindfulness training is still in its infancy, and many scientists are calling for more rigorous research methods such as standardized programs and better placebo-controlled designs. Yet the promise of mindfulness continues to generate much interest. The overarching message seems to be that the more time spent engaging in such training, the more benefits in attention. No matter our profession, as we learn to grab hold of our attention and become more meta-aware of our moment-to-moment experience, we gain the power to intervene in support of our own happiness and health. SA

Amishi P. Jha, author of the forthcoming book *Peak Mind* (HarperOne, October 2021), is a professor of psychology at the University of Miami, where she serves as director of contemplative neuroscience for the Mindfulness Research and Practice Initiative. Her research investigates the neural bases of attention, resilience and mindfulness.

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READY FOR ANYTHING

Scientists have compiled evidence-based tactics for building resilience. Among them: rethink adversity, forge close friendships and tackle novel challenges

By Steven M. Southwick and Dennis S. Charney

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As a college student at Brown University, Jerry White spent his junior year abroad studying in Israel. On a sunny day during the Passover holiday in April 1984, White and two friends set out for a camping trip in the Golan Heights. "I was walking out ahead of my friends with a song in my heart. I like being the leader, the one out in front," he recalls. "Then, boom! A huge explosion." He had stepped on a land mine. As blood poured from his leg, White screamed, "I have no foot! I have no foot!" White's friends wrapped his stump with a shirt, tied a makeshift tourniquet around the injured leg and carried him through what they now knew was a minefield. For the next four months White lived in two Israeli hospitals where he felt helpless, sad and alone. "People were trying to introduce themselves, but they were all missing arms, legs, eyes, or they were burn victims. I felt sick and afraid," he says.

Eventually White returned home, completed college and worked as a substitute teacher before becoming an activist working on behalf of fellow victims. In 1995 he, along with his friend and colleague Ken Rutherford, who had lost both legs to a land mine in Somalia, founded the Landmine Survivors Network (renamed Survivor Corps). This group played a leading role in the International Campaign to Ban Landmines, which was awarded the Nobel Peace Prize in 1997.

White's transformation from frightened victim to passionate survivor demonstrates resilience, the "process of adapting well in the face of adversity, trauma, tragedy, threats or significant sources of stress," according to the American Psychological Association. A resilient person may bend but does not break when confronted with adversity, enabling him or her to bounce back relatively quickly.

Biologically, resilience is the ability to modulate and constructively harness the stress response—a capacity essential to

WARTIME INJURIES need not be devastating. Many veterans learn and grow from their traumatic experiences.

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both physical and mental health. Unchecked, chronic stress can impair the immune system and contribute to illnesses such as gastric ulcers, asthma, depression, diabetes and heart disease. Stress can also spawn unhealthy behaviors such as smoking and excessive alcohol use.

Success appears to hinge on resilience. This is especially important during times of prolonged stress and suffering, such as the current COVID-19 pandemic. Setbacks are part of any human endeavor, and those who react to them productively will make the most progress.

Whether a person perseveres or gives up in hard times depends on influences at multiple levels, from molecules to neighborhoods. Resilience is determined by both inborn traits and environmental factors that affect the capacity to adapt to stress. Although some of these environmental influences, such as poverty, are difficult to alter, a person can increase his or her level of resilience by developing mental and physical habits that foster positive adaptation to stress and trauma.

RESILIENCE is critical to success. The ability to keep working toward a goal in the face of difficulty helps people in many types of professions thrive.

STANDING UP TO STRESS

BROWSE THROUGH the magazine section of any bookstore, and you will find an assortment of articles on how to reduce stress: "7 Rules for a Stress-Free Life," "Leave Your Stress Behind," "How You Can Reduce Your Stress and Your Dress Size," and so on. The basic message is that stress is bad—but it is not always. Some stress is actually good. Without stress, we would weaken. And difficulty that can be mastered facilitates growth, self-esteem, self-efficacy and resilience. A resilient person is thus not someone who avoids stress but someone who learns how to tame it.

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A body of data, including studies of identical twins, suggests that certain personal characteristics that foster resilience may be at least partly inherited. These traits include a temperament that leads a child to confidently take on novel tasks and interact with unfamiliar people, as well as a good-natured, sociable personality. Researchers are now uncovering some of the basic biology of resilience that facilitates our adaptive responses to stress [*see box on page 101*].

Beyond biology, a number of environmental variables affect resilience, among them family support, the stability and quality of schools, and the services in and safety of a neighborhood. For example, a loner who is unemployed will have more trouble dealing with stress and trauma than a financially secure individual in a supportive family. Weak leadership in a community and insufficient first-responder and financial resources can also compromise responses to adversity.

Some of these situational factors, along with specific character traits, may be hard to change. Nevertheless, people can learn to think and act in ways that greatly enhance resilience. Virtually anyone can become more resilient through disciplined, consistent practice. The more we activate specific brain areas through our behavior, the more neural connections form in those areas, enabling the neurons involved to transmit their messages more efficiently.

In our book *Resilience: The Science of Mastering Life's Greatest Challenges,* we identify 10 avenues for building resilience. Some of these strategies reduce stress. Others help you grow from the experience. Strategies to increase resilience include learning how to regulate your emotions, adopting a positive but realistic outlook, becoming physically fit, accepting challenges, maintaining a close and supportive social network, and observing and imitating resilient role models. We discuss each of these approaches below.

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ENGAGING in mindfulness meditation is an effective way of controlling stress.

EMOTIONAL RESCUE

THE ABILITY to regulate emotions such as sadness, anger and fear is critical for effectively coping with stress and trauma. Negative emotions are natural and often adaptive, but if left unchecked, they can seriously compromise our ability to think clearly and to make rational decisions in challenging situations.

Researchers have devised various strategies for regulating emotions and enhancing resilience. Two approaches that have received increasing scientific support in recent years are cognitive reappraisal and mindfulness meditation. Using reappraisal, individuals reinterpret the meaning of an adverse event so that they see it as less negative. Doing so tends to attenuate physiological and emotional reactions to the event. For example, psychologist Kevin Ochsner of Columbia University and his colleagues have shown that when people intentionally reinterpret a situation such as a rejection for a job as being less negative, they report a decrease in unpleasant emotions. Ochsner's team also found that this improvement in mood is accompanied by changes in the brain—in particular, an increase in activity in the prefrontal cortex, a center for planning, directing and inhibiting behavior, and a decrease in activity of the amygdala, a hub for feelings such as fear.

For years researchers have studied how people regulate their emotions. Individuals who frequently use cognitive reappraisal as a way to alter their emotional reactions to stress and trauma tend to report greater psychological well-being than those who do not look for neutral or positive ways to interpret their challenging circumstances. For example, in a 2008 study we, along with psychiatrist Adriana Feder and other colleagues at the Icahn School of Medicine at Mount Sinai, interviewed 30 former Vietnam prisoners of war about how they evaluated their wartime experiences. We found that most of these veterans, many of whom had been

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brutally tortured, had actively reappraised their imprisonment and found meaningful ways in which they had grown stronger, wiser and more resilient as a result of it. They also reported that they were now better able to see possibilities for the future, relate to others and appreciate life.

Training in cognitive reappraisal is a component of various therapies designed to enhance well-being, strengthen resilience and reduce distress. For example, cognitive-behavioral therapies, which are effective for treating mood and anxiety disorders, teach individuals to observe their own thoughts and behaviors, to challenge their negative assessments of stressful situations and of themselves, and to replace these with more realistic and positive points of view. When faced with a highly stressful or negative episode, you may find it helpful to ask yourself a few questions: "Is there a less destructive way to look at this situation?" "Am I catastrophizing or exaggerating its potential negative impact?" "Is there something that I can learn from this experience, or is it possible to grow stronger as a result?"

Another strategy for controlling stressful emotions is to engage in mindfulness meditation. This exercise teaches practitioners how to consciously live in the present moment rather than dwelling in the past or fretting about the future. The participant becomes an observer who learns to watch, but not judge, as the mind tends to automatically follow familiar conditioned patterns of thinking that often add to distress and maladaptive coping. Mindfulness meditation has been associated with improved ability to focus; more flexible thinking; greater psychological well-being; and better ability to cope with depression, anxiety and stress.

Brain-scanning experiments have revealed that both mindfulness meditation and training in cognitive reappraisal can increase activation of the left prefrontal cortex (a pattern associated with greater emotional control), which provides a boost in positive emotions and faster recovery from feelings such as anger, disgust and fear. Attending a workshop on mindfulness meditation is one good way to start learning how to modulate the stress response and successfully weather life's many challenges.

USING A COPING STRATEGY called **cognitive reappraisal, a person revises his or her interpretation of a difficult experience to make it less negative.**

A GLASS HALF FULL

IN ADDITION TO ATTENUATING negative emotions, a dedicated effort to bolster positive emotions can enhance a person's ability to bounce back from difficulty. Optimism and positive emotions are strongly associ-

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ated with good mental and physical health, even longevity. In a remarkable study published in 2001 developmental psychologist Deborah D. Danner of the University of Kentucky and her colleagues examined autobiographical sketches composed by 180 nuns from the School Sisters of Notre Dame in Milwaukee before they took their vows of commitment to the Church and God. They found that the degree of positive emotion expressed in the sketches, which had been written decades earlier, predicted longevity. Only 34 percent of nuns whose sketches were classified in the lowest quarter of cheerfulness were still alive at age 85, compared with 90 percent who had been classified in the most upbeat quarter.

The health benefits of positive emotions probably stem from a better ability to regulate the stress response. Psychologist Barbara L. Fredrickson of the University of North Carolina at Chapel Hill and her colleagues have found that negative emotions tend to increase physiological arousal, narrow our focus of attention and restrict our behaviors to those essential for survival. Positive emotions, in contrast, have been found to reduce arousal and broaden our focus, leading to more creative and flexible responses to stress and trauma.

Resilience is associated with realistic optimism, not the rose-colored form. Because the latter often involves ignoring negative information, people who adopt an overly buoyant outlook tend to underestimate stressful and risky situations, whereas realistic optimists filter out unnecessary negative information but pay close attention to bad news that is relevant to dealing with adversity. To enhance optimism, focus on what is positive around you, intentionally think positive thoughts, embrace humor, reframe the negative in a more positive light, behave in ways that are known to be associated with positive emotions, and try to associate with positive friends and colleagues—emotions can be contagious.

EXERCISE can strengthen attention, decision-making and memory, empowering people to better shoulder stress.

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WORKING OUT YOUR TROUBLES

PHYSICAL ACTIVITY can enhance resilience by protecting people (and animals) against the negative effects of stress. During the past two decades neuroscientist Benjamin N. Greenwood of the University of Colorado Denver and his colleagues have published a series of studies in rats showing that weeks of voluntary wheel-running exercise can ward off anxiety and depression-like behaviors, such as exaggerated fear, reduced social exploration and increased intake of morphine, that can result from exposure to a variety of intense stressors.

In humans, aerobic exercise also has been shown to reduce symptoms of depression and anxiety. It improves attention, planning, decision-making and memory, all of which are important for effectively managing stress. Exercise appears to promote resilience through a number of neurobiological mechanisms. For example, it boosts levels of endorphins and of neurotransmitters such as dopamine and serotonin that may reduce symptoms of depression and elevate mood. It also suppresses the release of the stress hormone cortisol.

In addition, workouts seem to activate genes encoding proteins such as brain-derived neurotrophic factor (BDNF) that promote the growth and repair of neurons, which prolonged stress can damage. In a study published in 2011 psychologist Arthur F. Kramer, then at the University of Illinois at Urbana-Champaign, and his colleagues found that moderate-intensity aerobic exercise (three days a week for one year) increased the size of the hippocampus, a brain region that is involved in

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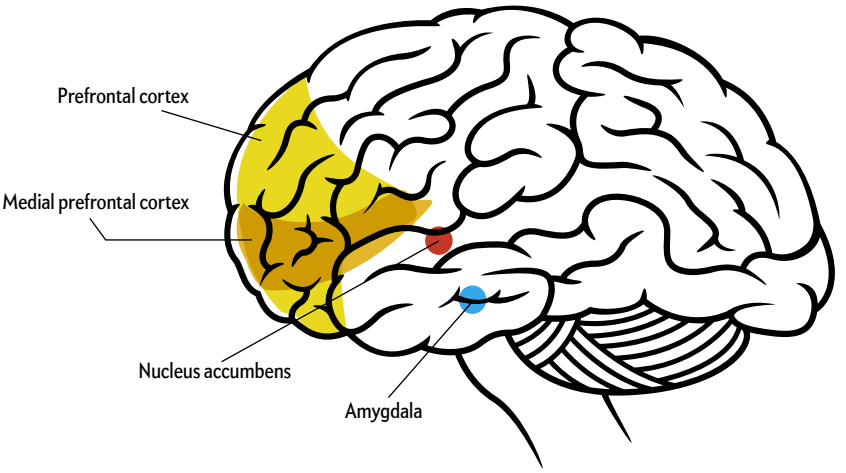
The Biology of Bouncing Back



Researchers have traced resilience, the capacity to recover from adversity, to a network of brain regions and chemicals. Beginning early in one's life, an individual's genes and the interaction of those genes with the environment shape brain circuits that underlie the psychological strengths and behaviors of resilient people.

Epigenetics helps to explain how the environment influences our genes. Our genes carry instructions for assembling every cell of our body. But the environment, including our behaviors, can change how genes are expressed. Stimuli such as fear, diet and social support can trigger biochemical reactions that turn genes on or off. Thus, genes are not destiny, and the degree to which they influence our lives might depend on our environment.

Critical to building resilience is the capacity to face fears, experience positive emotions, search for adaptive ways to reframe stressful events and benefit from relationships. Thus, resilience relies on neural circuits governing fear, reward, and social and emotional regulation. These circuits overlap at certain brain structures. For example, the amygdala not only regulates fear but also plays a major part in reward, through the processing of positive emotions. The nucleus accumbens, the hub of reward, also influences social behaviors such as sociability and pair bonding. The medial prefrontal cortex has a role in all three circuits, helping to regulate social interactions and emotions and relaying that information to other regions to inform higher-level decisions. As a result of the overlap and connections among these circuits, how a person faces fear is correlated with his or her ability to remain upbeat under stress and generate rewarding social experiences in tough times.

The neural circuits of fear, reward and social behaviors are powered by a variety of neurochemicals and hormones. One of these, neuropeptide Y, is a short protein found in the amygdala and other regions that mediate anxiety and fear. Among people under severe stress, such as someone undergoing challenging military training, higher neuropeptide Y levels are connected to better performance. High levels of the stress hormone cortisol, however, are associated with depression. Norepinephrine, another stress hormone, helps us react appropriately to danger by readying us to fight or flee the scene. Unrestrained repeated increases in norepinephrine may create chronic anxiety, however. Dopamine and serotonin, meanwhile, help us stay positive under difficult conditions.

Resilience may also be related to activation of the left prefrontal cortex. When active, this region at the surface of the brain just behind the forehead sends inhibitory signals to the amygdala, quieting anxiety and fear-based emotions, and leaving the frontal brain region free to plan and set goals. In this way, individuals are better able to persevere, maintain a positive self-image, remain hopeful in stressful times, and regulate their stress response so that it is deactivated when no longer needed. Understanding the biological underpinnings of resilience could help researchers and clinicians design psychological and pharmacological interventions that make people better able to overcome adversity. —*S.M.S. and D.S.C.*

both memory and stress regulation, by 2 percent. This growth was associated with increases in BDNF levels and improved memory, suggesting that exercise can protect neurons in this area and may therefore help people recover from difficult circumstances.

For general health, the Department of Health and Human Services has recommended at least one hour and 15 minutes a week of intense aerobic workouts such as swimming or running or twice as much moderately intense exercise—mowing the lawn, say, or walking fast—along with two days of muscle strengthening. (Those who work out more tend to reap greater health benefits, although very intense or prolonged athletic endeavors can actually be detrimental to physical and mental health.)

To enhance resilience, however, we recommend that you consult with your physician and then develop a schedule in which you gradually increase the intensity of your cardiovascular and strength training. Every workout should be challenging but manageable. In this way, in addition to getting the biological benefits of exercise itself, you are also carefully calibrating your exposure to stress in a way that is known to increase resilience.

This general strategy is called stress inoculation. It is based on the notion that if a person deliberately takes on increasingly difficult challenges, he or she will gradually learn to handle higher levels of stress. The inoculation principle of graded exposure can apply to a broad range of activities designed to increase physical, emotional and cognitive resilience. For exam-

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FRIENDSHIPS can lift you up, provide security and prevent a precipitous fall.

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ple, practitioners of mindfulness can increase their ability to concentrate by gradually lengthening their periods of meditation. A person who is afraid to give speeches might sign up for a public speaking workshop and afterward accept speaking engagements in front of small, nonthreatening audiences, then gradually agree to stand up in front of larger and more challenging crowds.

Such experiences should be outside your comfort zone but not so intense as to be unmanageable or potentially harmful. You should also plan to progressively increase the intensity or difficulty of these endeavors. As noted in the *U.S. Army Combat Stress Control Handbook,* "to achieve greater tolerance or acclimatization to a physical stressor, a progressively greater exposure is required. The exposure should be sufficient to produce more than the routine stress reflexes.… In other words you must stress the system." Moreover, make training as realistic as possible. Pilots, firefighters, police and soldiers all enhance their physical, cognitive and emotional skills in realistic training settings where they can obtain constructive feedback from instructors and colleagues.

As you acclimate to greater levels of stress, you will need to recover and relax more. Psychologist James Loehr, who has written books on resilience training, points out that insufficient recovery relative to the high volume of stress can be quite damaging. One of the most important life skills may be knowing when high recovery needs to balance high stress.

FRIENDS IN NEED

A PARTICULARLY EFFECTIVE way to enhance resilience is to strengthen your relationships because doing so can dampen your biological response to stress and bolster your courage in tense situations. High levels of social support have been associated with better psychological outcomes after many types of trauma, including childhood sexual abuse and combat. High social support has also been linked with protection against depression and stress disorders such as PTSD, as well as greater emotional well-being and longer life. In contrast, social isolation has a negative impact on psychological and physical health, with effects on longevity similar to those of a sedentary life style, obesity or cigarette smoking.

Backing from others is powerful because it increases an individual's self-confidence, provides a safety net if we should fall and bolsters our belief that we can overcome obstacles. As a result, we tend to more actively solve problems rather than passively avoiding challenges. After all, bonding with others does provide greater security; a group that works closely together is stronger than an indi-

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TAKING ON moderately stressful challenges, such as giving a lecture in front of a small group, can boost resilience.

vidual. On a biological level, social ties activate the parasympathetic nervous system, which lowers subjective and physiological measures of stress and prompts the release of the hormone oxytocin. Oxytocin is known to reduce anxiety and fear, in part by limiting the cortisol response to stress. (It also promotes affiliative behaviors and emotions, such as trust, that encourage continued socializing.)

Interestingly, social support may have an even stronger effect on coping with adversity in Latin American and other cultures that place great value on interdependence, extended kinship systems and collectivism. It plays a comparatively lesser role in more individualistic cultures, although relationships in all societies are vital.

To boost resilience through your relationships, first evaluate your social network. Make a list of the people you feel connected to. With whom do you interact daily? Who would help you without hesitation? To whom do you turn for advice? Who really understands you? Resilience is strongly associated with altruism and giving support to others.

If you find you need to bolster or simply maintain a supportive network, reach out to family, friends and colleagues. Join organizations that share your interests and concerns. Find ways to help others. As an adult, it is also important to teach kids the skills needed to become socially competent, such as knowing how to listen to and empathize with others.

MORE THAN FLATTERY

IN YOUR SOCIAL CIRCLES, look for people who recover quickly from hardship whom you could learn from. Members of your own family, colleagues, teachers, coaches, or even historical figures or fictional characters could also serve as resilient role models.

Psychologist Albert Bandura, a highly influential emeritus professor at Stanford University, believes that modeling is most effective when the observer has analyzed what he or she wishes to imitate by dissecting it into segments and creating rules that could guide future action. For example, when a friend lost her job, we noticed that she immediately called fellow employees, former employers and friends to solicit their help in searching for a new position. When she fell ill with pneumonia, she moved in with her sister until she recovered. And when her mother died, she called her family and closest friends and asked them to spend time with her. Rather than going it alone in times of stress, she reached out for support from those who care about her, a pattern that can guide our own behavior. Other resilience-enhancing attitudes and behaviors include perseverance and endurance, moral character and virtues, toughness tempered by compassion, altruism, dignity in the face of deprivation and potential growth from suffering.

The resilience-enhancing strategies described above can be powerful tools for dealing with life's challenges, including the COVID-19 pandemic. This pandemic has caused unprecedented levels of stress, trauma and depression among the general public and among frontline health-care workers, who have risked their own lives to save the lives of their patients.

White, the land-mine survivor, is an outstanding model of resilience. Through years of soul-searching (read: cognitive reappraisal), he began to see the loss of his foot as more opportunity than horrendous misfortune. Together with a group of like-minded individuals, he embarked on a quest to rid the world of land mines. Through thoughtful reassessment, social support and a problem-solving approach, White transformed his tragedy into a mission of hope.

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OPINION

MENTAL HEALTH AFTER COVID

In the wake of the pandemic, there will be an even greater need for help in the face of loss, isolation and trauma

By Sofia Noori and Isobel Rosenthal

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AS PSYCHIATRISTS WHO HAVE WORKED ON THE FRONT LINES OF THE pandemic, we've seen firsthand how the COVID-19 outbreak has ruthlessly tested the limits of our health-care system. Just as the pandemic seemed to be momentarily abating, the country began reckoning with another public health crisis—that of anti-Black racism and police violence. Data show that COVID disproportionately affects minority communities, likely resulting from racism's downstream effects on socioeconomic opportunities, health outcomes and insurance coverage.

With widespread social isolation, high unemployment and unprecedented levels of stress, we are witnessing an impending mental health crisis. Although these events have painfully unearthed the weaknesses of our system, we as psychiatrists see one hopeful prospect: recognition and improvement of mental health care in the U.S. Here are five ways that we believe COVID could drive mental health innovation forward to create a more equitable system of care for Americans.

THE POWER OF TELEHEALTH

MENTAL HEALTH CLINICS across the country shut down in-person services at the start of the pandemic, leading to a huge rise in utilization of telemedicine solutions. Remarkably, patients and clinicians alike have discovered that this form of clinical interaction can work and may even be preferable in some scenarios. Telehealth practice solutions such as Doxy.Me and Zoom For Healthcare, as well as start-ups such as Teladoc and Talkspace, have seen dramatic increases in demand.

Fueling the transition is the loosening of telehealth regulations. The Centers for Medicare and Medicaid Services (CMS) began temporarily reimbursing telehealth at the same rate as in-person treatment. "Originating site requirements," which require patients to be located at a health-care facility to participate in telehealth visits, were suspended in 2020. States also eased licensure requirements so that physicians could practice across state lines. An increasing number of telephonic visits are being reimbursed as well, and HIPAA enforcement is being relaxed so physicians can videoconference with their patients without excess worry.

Although telehealth reimbursement may begin to decrease as in-person visits resume, we predict that some regulations will stay loosened as its prominence increases. In fact, some telehealth coverage was made permanent at the end of 2020. The Medicare originating site requirement, considered overly restrictive by many, may be dropped permanently. As patients and clinicians alike see the value of telehealth, its steadily increasing market share may be the easiest trend to spot in mental health care.

SUBSTANCE USE RESOURCES

PEOPLE WITH SUBSTANCE USE disorders (SUDs) are especially suffering from disruption to their treatment. Mainstays, including peer support groups, counseling sessions and periodic toxicology screens, are all severely interrupted. During the 2008 Great Recession, social isolation and economic depression led to a wave of opioid and illicit drug use that fueled the opioid epidemic. As we navigate another recession, many health-care professionals are particularly worried about their clients relapsing or increasing their use.

Thankfully, technology has enabled in-home

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access to substance use supports. Peer support groups such as AA and Smart Recovery are operating nearly all of their groups through video, and methadone clinics are now able to dispense weeks of methadone to clients. Buprenorphine, another medication-assisted therapy for opiate use disorder, can now initially be prescribed online. Online substance use programs, such as Lionrock Recovery, have seen demand rise by more than 40 percent. Even as some communities reopen clinical services, there will still be intense market pressure for comprehensive home-based solutions to substance use treatment.

CONTINUUM OF CARE

A HUGE PROBLEM in U.S. behavioral health care is the lack of intermediate care options. In the continuum of care, treatment resources cluster around outpatient treatment, such as weekly therapy with a counselor, and inpatient treatment, such as admission to a psychiatric hospital. Intermediate care options such as intensive outpatient programs (IOPs) and partial hospital programs (PHPs) offer a way for patients to be engaged in intensive therapy, medication management and group support, but they do not require patients to be admitted for a costly hospitalization.

Across the country many IOPs and PHPs have converted to telehealth because of COVID. In New York State, strict billing requirements that were associated with PHPs and prevented their widespread availability have been loosened. We believe that online intermediate care models should continue outside of this pandemic, especially for patients in rural states where access to such care traditionally lagged. The demand for intermediate care options that increase outpatient support and prevent hospital admissions will expand the menu of treatment options past simple weekly therapy.

PERSONALIZED DATA

TO PLACE SOMEONE in the appropriate treatment option, we must be able to quantify a person's risk and needs. Mental health providers are traditionally bad at predicting or quantifying risk, including suicide risk. Part of this inability to assess risk has been the historical struggle with the implementation of measurement-based care, defined as the ability to quantify symptoms of patients with mental illness. The COVID-19 crisis and the increasing utilization of digital tools can help researchers discover new markers of impending decompensation. We can also better understand the types of digital tools that people find effective for their mental health treatment. We hope that this information will help us to develop risk-informed treatment plans and more precise delivery of care.

INTRODUCING PUBLIC MENTAL HEALTH

PUBLIC MENTAL HEALTH FOCUSES on preventing mental illness instead of simply treating it. Because COVID can be classified as a collective trauma, Americans are at risk of developing post-traumatic stress from the pandemic. Compounded with the inequitable outcomes we are seeing across Black and brown communities, we may be worsening our existing mental health disparities. The mental health consequences of COVID could lead to long-term losses in well-being, diminished economic productivity and increasing health-care costs. Unfortunately, the existing U.S. mental health system is sorely lacking a public focus: it engages largely with those who are already mentally ill and often only those who are able to pay for treatment.

We believe that to reduce long-term economic and social impact, payers and government will need to increase funding of public mental health programs that prevent illness and increase treatment access. To be effective, these programs must offer access to those without financial resources or with serious mental illness and commit to best practices when treating underserved populations. Tech-enabled services that can assist with risk stratification, offer support before illness develops, or connect people with accessible mental health treatment are slowly arriving, joining those such as NYC Well, which offers a "front door" to support services for New Yorkers in mental duress. For tech-enabled solutions to soar, however, structural change that closes the gaps in funding and infrastructure must occur.

PUBLIC MENTAL HEALTH FOCUSES ON PREVENTING MENTAL ILLNESS INSTEAD OF SIMPLY TREATING IT. BECAUSE COVID CAN BE CLASSIFIED AS A COLLECTIVE TRAUMA, AMERICANS ARE AT RISK OF DEVELOPING POST-TRAUMATIC STRESS FROM THE PANDEMIC.

In the midst of the devastation, we remain hopeful that mental health care will transform. As the U.S. confronts a calamitous loss of life, widespread isolation and deep social fractures, there will be an even greater need for mental health services. A functioning mental health-care system will be critical in supporting our communities. SA

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OPINION

The Coronavirus and Post-Traumatic Growth

Surviving an awful experience can lead to some surprisingly positive psychological effects in many people

By Steve Taylor

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ON MARCH 6, 1987, A FERRY TRAVELING FROM ENGLAND to Belgium capsized, resulting in the death of 193 people. In the months after the disaster, many of the approximately 300 survivors suffered symptoms of post-traumatic stress disorder, including upsetting dreams, anxiety, emotional detachment and numbness, and difficulties with sleep and concentration.

In time, however, some of the survivors reported some surprising positive effects. Three years after the disaster, psychologist Stephen Joseph, then a Ph.D. student, carried out a survey that found that, although PTSD was still common (albeit with diminished symptoms), 43 percent of the survivors said their view of life had changed for the better. They reported that they no longer took life for granted, that they valued their relationships more, that they lived each day to the fullest, that they felt more experienced about life, and so on.

This was one of the first studies of a concept that has become very important in psychology in recent years: post-traumatic growth.

Post-traumatic growth is the idea that, in the long run, traumatic events and experiences—such as illness, accidents, bereavement, addiction and divorce—can have beneficial effects. Often after the initial shock and pain of a traumatic situation has faded away, people report feeling more appreciative of their lives and sensing a new inner strength and confidence. They feel that their relationships are more intimate and authentic and that they have a new sense of meaning and purpose. They often become less materialistic and more altruistic, more concerned with the well-being of others than with their own success and status. They develop a more philosophical or spiritual attitude to life, with—in the words of Richard Tedeschi and Lawrence Calhoun, two of the pioneers of the theory of post-traumatic growth—a "deeper level of awareness."

Overall it appears that nearly half of people who experience such traumatic events are likely to experience post-traumatic growth in the aftermath.

POST-TRAUMATIC TRANSFORMATION

OVER THE PAST 10 YEARS or so my own research has focused on what I call post-traumatic transformation. I have found that psychological turmoil and trauma may bring about not simply growth but a dramatic transformation. After a period of intense suffering (such as a diagnosis of cancer or a long period of depression or addiction), a person may undergo a sudden shift of identity.

All of a sudden, they feel like a different person inhabiting the same body, with heightened sensory awareness, an increased sense of compassion and connection, and new values or goals. For example, a woman who experienced post-traumatic transformation after the death of her daughter told me that she felt like she had broken through "to another state. I've moved up to another level of awareness, which I know is going to stay with me."

As I showed in my book *The Leap,* many people could specify a particular moment at which transformation occurred, often at the moment when they shifted into an attitude of acceptance of their predicament. For example, a man told me how, as an alco-

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holic undergoing the Alcoholics Anonymous recovery process, he experienced transformation at the moment when he "handed over" his problem. Another person had become severely disabled and underwent a shift at the point when he heard an inner voice say, "Let go, man, let go. Look at how you're holding on. What do you think life's telling you?" A woman who went through a period of intense postnatal depression entered into a psychotic state, which led to four nights without sleep. In the midst of this turmoil, she had an argument with her husband, which suddenly triggered what she described as "feelings of such perfect joy and peace. I remember thinking afterward, 'So that's what I'm supposed to feel like!' Within that one instant, you are forever changed."

TRANSFORMATION OF COMMUNITIES

POST-TRAUMATIC GROWTH (and post-traumatic transformation) can happen to groups and communities, as well as to individuals.

When a crisis occurs in a community (such as a war or a natural disaster), people often react by becoming more interconnected. They become friendlier, more cooperative and altruistic. People feel a common sense of purpose, and a spirit of cooperation begins to replace normal competitiveness. For the community, this often equates to a kind of post-traumatic growth. The entire community shifts into a higher level of integration. It is as if, rather than existing as isolated individuals, people fuse together into a whole. One study showed evidence of collective post-traumatic growth after natural disasters such as earthquakes and floods. In these situations, people developed communal coping strategies and had more collective gatherings.

I witnessed this phenomenon about four years ago, following a terrorist attack in my home city of Manchester, England (in which 23 people died when a man detonated a homemade bomb at a train station). In the days and weeks after the attack, there was a strong sense of togetherness. People were talking more and helping one another more. Different ethnic groups were interacting more. Barriers and boundaries seemed to fall away. There was a sense of trust and empathy in the community. Eventually the sense of togetherness began to wane, but I don't think it has faded away completely. I think the event brought about a new kind of integration that is still present today, at least to a degree.

POST-TRAUMATIC GROWTH AND THE PANDEMIC

THIS DOESN'T ALWAYS HAPPEN, of course. Sometimes crises can have the opposite effect and lead to a kind of post-traumatic stress in which social bonds fall away and people become more selfish and individualistic. Perhaps communal post-traumatic growth following a crisis is roughly as common as individual post-traumatic growth.

Yet my feeling is that post-traumatic growth will be one of the aftereffects of the coronavirus epidemic. Many of us will surely undergo individual growth (and perhaps even transformation). In the midst of the suffering and challenges of our present predicament, we may develop a heightened sense of appreciation, more authentic relationships, and a new sense of resilience and confidence. We may slow down and learn to live in the present rather than filling our lives with incessant activity and constantly rushing into the future.

And we will surely undergo some degree of communal growth. In the U.K., there are signs that this is happening already. People appear to be valuing others more, appreciating the different contributions we are making and letting go of grievances and disagreements. Despite social distancing, we appear to be feeling more empathy for one another and are acting more altruistically. In Manchester, I can sense the same spirit of togetherness that arose after the terrorist attack.

WHEN A CRISIS OCCURS IN A COMMUNITY (SUCH AS A WAR OR A NATURAL DISASTER), PEOPLE OFTEN REACT BY BECOMING MORE INTERCONNECTED.

But perhaps post-traumatic growth will occur at an even higher level, too—that is, at a global level. One of the most salient aspects of the virus is its global nature. It reminds us that we are one species and that differences of nationality, ethnicity and religion are meaningless labels. We are all in this together, and we will overcome the crisis only through cooperation. Conflict and competition will only lead to more suffering and discord.

During a time of increasing individualism in which many governments have been taken over by narcissistic and sociopathic autocrats intent on asserting their own individual power and identity, post-traumatic growth up to the global level is precisely what the world needs.

When this is all over, we may find that we are stronger and closer to one another than before. SA

Steve Taylor is a senior lecturer in psychology at Leeds Beckett University in England. He is author of *Spiritual Science: Why Science Needs Spirituality to Make Sense of the World.*

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A Psychological First Aid Kit

Simple skills might ease a COVID mental health crisis

By the Editors

As soon as Joe Biden was elected U.S. president, he made his priorities clear by appointing a panel of distinguished experts to advise him on the coronavirus pandemic. The panel has members who are helping the new administration organize vaccine distribution to millions of people and help millions of others who need to be protected until they can get the vaccine. These experts are weighing in on preventive strategies to minimize the likelihood of infection and advise on treatments that can reduce the severity of the disease in those who get sick.

But there is also a need to address a related problem. For months a mental health crisis has accompanied the misery brought on by COVID-19. The U.S. Centers for Disease Control and Prevention reported last August that symptoms of anxiety had tripled and depression symptoms had quadrupled among a group of 5,470 adults as compared with a survey sample from 2019. Meanwhile mental health services have been stretched worldwide. One reason is that mental health personnel and the facilities they work in have been reassigned to COVID-related tasks during the crisis.

All of us need to sustain and enhance our psychological resilience to weather the daily toll of activity restrictions, rising case numbers, hospitalizations and deaths. A set of simple measures known as psychological first aid or mental health first aid can enable people to help family, friends and others in their communities who experience psychological distress from pandemic fatigue, COVID convalescence, or the loss of a friend or relative.

These techniques allow people to become mental health first responders. An analogy to a Red Cross first aid course is apt: both teach trainees what to do when arriving first at the scene—and also flag actions to be avoided. A physical first-aider tries to stabilize the patient; with psychological first aid, a key goal is to restore a person's sense of safety. If someone is terrified that ordinary (and mental health–building) activities such as going outside are fraught with danger, for example, the responder might mention that air currents and sunlight reduce the risk of becoming ill, offering reassurance that being outdoors during a pandemic could be less hazardous than remaining isolated inside.

What the responder does *not* say is equally important. When dealing with a person suffering from a panic attack because of a recent trauma, the first-aider might discourage conversation about the details of the event to avoid reinforcing the memory. Other items on a to-do list might include promoting a feeling of "self-efficacy," or confidence that the person in crisis has the capability to cope with the situation at hand, such as meeting basic needs for food and shelter and establishing contact with family or a mental health professional as needed.

Psychological first aid was used during the SARS and Ebola epidemics. Social service agencies at every level of government and the nonprofit sector should provide more support now for first aid for the psyche because the need has exploded as a result of COVID. Before its arrival, most psychological first aid students at the Institute for Disaster Mental Health at the State University of New York at New Paltz were public safety and health-care workers. But by late 2020 instructors were teaching librarians, who have become frequent confidantes to patrons experiencing extreme stress.

One trainer in the town of Marshfield, England, offered anyone who lives or works there free four-hour courses in mental health first aid because of the prevalence of pandemic-related distress. Mental health first aid is slightly different from psychological first aid because it is targeted at people experiencing issues even before a crisis erupts. The method, created by two educators in Australia, has been taught to 3.6 percent of that nation's 25 million citizens—and its inventors are eager to reach 10 percent, which would match or exceed the country's first aid trainees for physical injuries.

Biden's coronavirus task force needs to do its part by taking the mental pain from pandemic fatigue into account in its national plan for COVID-19. It should recognize that modest but readily achievable efforts such as teaching psychological first aid and other forms of resilience training may have a big impact over a short time. But you may not have to wait on the new administration or your local government. Psychological first aid is accessible now—people can learn it online for free through a Coursera curriculum developed by the Johns Hopkins Center for Public Health Preparedness. Everyone should take it. SA

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